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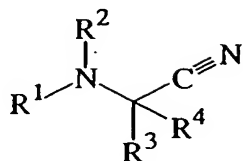
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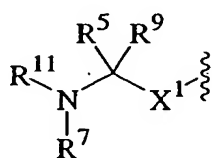
1. A compound of Formula (I):



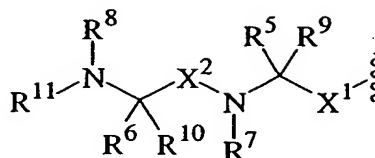
(I)

in which:

- 5  $\text{R}^1$  is a group of Formula (a) or (b):



(a)



(b)

wherein:

$\text{X}^1$  and  $\text{X}^2$  independently are  $-\text{C}(\text{O})-$  or  $-\text{CH}_2\text{S}(\text{O})_2-$ ;

$\text{R}^5$  and  $\text{R}^6$  are hydrogen or  $(\text{C}_{1-6})$ alkyl;

- 10  $\text{R}^7$  and  $\text{R}^8$  are hydrogen or  $(\text{C}_{1-6})$ alkyl or as defined below;

$\text{R}^9$  and  $\text{R}^{10}$  independently are (i)  $(\text{C}_{1-6})$ alkyl optionally substituted with cyano, halo or nitro or (ii) a group selected from  $-\text{X}^3\text{NR}^{12}\text{R}^{12}$ ,  $-\text{X}^3\text{NR}^{12}\text{C}(\text{O})\text{OR}^{12}$ ,  $-\text{X}^3\text{NR}^{12}\text{C}(\text{O})\text{NR}^{12}\text{R}^{12}$ ,  $-\text{X}^3\text{NR}^{12}\text{C}(\text{NR}^{12})\text{NR}^{12}\text{R}^{12}$ ,  $-\text{X}^3\text{OR}^{12}$ ,  $-\text{X}^3\text{SR}^{12}$ ,  $-\text{X}^3\text{C}(\text{O})\text{OR}^{12}$ ,  $-\text{X}^3\text{C}(\text{O})\text{NR}^{12}\text{R}^{12}$ ,  $-\text{X}^3\text{S}(\text{O})_2\text{NR}^{12}\text{R}^{12}$ ,  $-\text{X}^3\text{P}(\text{O})(\text{OR}^{12})\text{OR}^{12}$ ,  $-\text{X}^3\text{OP}(\text{O})(\text{OR}^{12})\text{OR}^{12}$ ,  $-\text{X}^3\text{NR}^{12}\text{C}(\text{O})\text{R}^{13}$ ,  $-\text{X}^3\text{S}(\text{O})\text{R}^{13}$ ,  $-\text{X}^3\text{S}(\text{O})_2\text{R}^{13}$ ,  $-\text{X}^3\text{C}(\text{O})\text{R}^{13}$ ,  $-\text{X}^3\text{C}(\text{O})\text{R}^{14}$ ,  $-\text{X}^3\text{C}(\text{O})\text{OR}^{14}$ ,  $-\text{X}^3\text{OC}(\text{O})\text{R}^{14}$ ,  $-\text{X}^3\text{NR}^{15}\text{C}(\text{O})\text{R}^{14}$ ,  $-\text{X}^3\text{NR}^{15}\text{C}(\text{O})\text{OR}^{14}$ ,  $-\text{X}^3\text{C}(\text{O})\text{NR}^{14}\text{R}^{15}$ ,  $-\text{X}^3\text{S}(\text{O})_2\text{NR}^{14}\text{R}^{15}$ ,  $-\text{X}^3\text{NR}^{15}\text{C}(\text{O})\text{NR}^{14}\text{R}^{15}$ ,  $-\text{X}^3\text{NR}^{15}\text{C}(\text{NR}^{15})\text{NR}^{14}\text{R}^{15}$ ,  $-\text{X}^4\text{SR}^{14}$ ,  $-\text{X}^4\text{S}(\text{O})\text{R}^{14}$ ,  $-\text{X}^4\text{S}(\text{O})_2\text{R}^{14}$ ,  $-\text{X}^4\text{OR}^{14}$ , or  $-\text{X}^4\text{NR}^{14}\text{R}^{15}$ , wherein  $\text{X}^3$  is  $(\text{C}_{1-6})$ alkylene,  $\text{X}^4$  is a bond or  $(\text{C}_{1-6})$ alkylene,  $\text{R}^{12}$  at each

occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl, R<sup>13</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl, R<sup>14</sup> is (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>8-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl and R<sup>15</sup> is hydrogen or (C<sub>1-6</sub>)alkyl, and wherein within R<sup>14</sup> said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a group selected from -R<sup>16</sup>, -X<sup>4</sup>OR<sup>16</sup>, -X<sup>4</sup>SR<sup>16</sup>, -X<sup>4</sup>S(O)R<sup>16</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>16</sup>, -X<sup>4</sup>C(O)R<sup>16</sup>, -X<sup>4</sup>C(O)OR<sup>16</sup>, -X<sup>4</sup>OC(O)R<sup>16</sup>, -X<sup>4</sup>NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)R<sup>16</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)OR<sup>16</sup>, -X<sup>4</sup>C(O)NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>S(O)<sub>2</sub>NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)NR<sup>16</sup>R<sup>17</sup> or -X<sup>4</sup>NR<sup>17</sup>C(NR<sup>17</sup>)NR<sup>16</sup>R<sup>17</sup>, wherein X<sup>4</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>16</sup> is hydrogen or (C<sub>1-6</sub>)alkyl and R<sup>17</sup> is (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>8-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl, or (iii) a group selected from (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl and hetero(C<sub>8-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl, wherein said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a group selected from -R<sup>16</sup>, -X<sup>4</sup>OR<sup>16</sup>, -X<sup>4</sup>SR<sup>16</sup>, -X<sup>4</sup>S(O)R<sup>16</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>16</sup>, -X<sup>4</sup>C(O)R<sup>16</sup>, -X<sup>4</sup>C(O)OR<sup>16</sup>, -X<sup>4</sup>OC(O)R<sup>16</sup>, -X<sup>4</sup>NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)R<sup>16</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)OR<sup>16</sup>, -X<sup>4</sup>C(O)NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>S(O)<sub>2</sub>NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)NR<sup>16</sup>R<sup>17</sup> or -X<sup>4</sup>NR<sup>17</sup>C(NR<sup>17</sup>)NR<sup>16</sup>R<sup>17</sup>, wherein X<sup>4</sup>, R<sup>16</sup> and R<sup>17</sup> are as defined above; wherein within R<sup>9</sup> and/or R<sup>10</sup> any alicyclic or aromatic ring system present may be substituted further by 1 to 5 radicals independently selected from (C<sub>1-6</sub>)alkyl, (C<sub>1-6</sub>)alkylidene, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro, -X<sup>4</sup>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>OR<sup>12</sup>, -X<sup>4</sup>SR<sup>12</sup>, -X<sup>4</sup>C(O)OR<sup>12</sup>, -X<sup>4</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>P(O)(OR<sup>4</sup>)OR<sup>12</sup>, -X<sup>4</sup>OP(O)(OR<sup>12</sup>)OR<sup>12</sup>, -X<sup>4</sup>OC(O)R<sup>13</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)R<sup>13</sup>, -X<sup>4</sup>S(O)R<sup>13</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>13</sup> and -X<sup>4</sup>C(O)R<sup>13</sup>, wherein X<sup>4</sup>, R<sup>12</sup> and R<sup>13</sup> are as defined above, or

R<sup>9</sup> taken together with R<sup>7</sup> and/or R<sup>10</sup> taken together with R<sup>8</sup> form

trimethylene, tetramethylene or phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene; and

$R^{11}$  is  $-X^5X^6R^{18}$ , wherein  $X^5$  is  $-C(O)-$ ,  $-C(O)C(O)-$  or  $-S(O)_2-$ ,  $X^6$  is a bond,  $-O-$  or  $-NR^{19}-$ , wherein  $R^{19}$  is hydrogen or  $(C_{1-6})$ alkyl, and  $R^{18}$  is

(i)  $(C_{1-10})$ alkyl optionally substituted by cyano, halo, nitro,  $-NR^{12}R^{12}$ ,  $-NR^{12}C(O)OR^{12}$ ,  $-NR^{12}C(O)NR^{12}R^{12}$ ,  $-NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-OR^{12}$ ,  $-SR^{12}$ ,  $-C(O)OR^{12}$ ,  $-C(O)NR^{12}R^{12}$ ,  $-S(O)_2NR^{12}R^{12}$ ,  $-P(O)(OR^{12})OR^{12}$ ,  $-OP(O)(OR^{12})OR^{12}$ ,  $-NR^{12}C(O)R^{13}$ ,  $-S(O)R^{13}$ ,  $-S(O)_2R^{13}$ ,  $-C(O)R^{13}$ ,  $-OR^{20}$ ,  $-SR^{20}$ ,  $-S(O)R^{20}$ ,  $-S(O)_2R^{20}$ ,  $-C(O)R^{20}$ ,  $-C(O)OR^{20}$ ,  $-C(O)NR^{20}R^{21}$ ,  $-NR^{20}R^{21}$ ,  $-NR^{21}C(O)R^{20}$ ,  $-NR^{21}C(O)OR^{20}$ ,  $-NR^{21}C(O)NR^{20}R^{21}$  or  $-NR^{21}C(NR^{21})NR^{20}R^{21}$ , wherein  $R^{12}$  and  $R^{13}$  are as defined above,  $R^{20}$  is  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  $(C_{9-12})$ bicycloaryl $(C_{0-6})$ alkyl or hetero $(C_{8-12})$ bicycloaryl $(C_{0-6})$ alkyl and  $R^{21}$  at each occurrence independently is hydrogen or  $(C_{1-6})$ alkyl, or

(ii)  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  $(C_{9-12})$ bicycloaryl $(C_{0-6})$ alkyl or hetero $(C_{8-12})$ bicycloaryl $(C_{0-6})$ alkyl or (iii)  $(C_{3-6})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-6})$ cycloalkyl $(C_{0-6})$ alkyl, phenyl $(C_{0-6})$ alkyl or hetero $(C_{5-6})$ aryl $(C_{0-6})$ alkyl, wherein said cycloalkyl, heterocycloalkyl, phenyl or heteroaryl is substituted by  $-X^4OR^{22}$ ,  $-X^4SR^{22}$ ,  $-X^4S(O)R^{22}$ ,  $-X^4S(O)_2R^{22}$ ,  $-X^4C(O)R^{22}$ ,  $-X^4C(O)OR^{22}$ ,  $-X^4C(O)NR^{22}R^{23}$ ,  $-X^4NR^{22}R^{23}$ ,  $-X^4NR^{23}C(O)R^{22}$ ,  $-X^4NR^{23}C(O)OR^{22}$ ,  $-X^4NR^{23}C(O)NR^{22}R^{23}$  or  $-X^4NR^{23}C(NR^{23})NR^{22}R^{23}$ , wherein  $X^4$  is as defined above,  $R^{22}$  is  $(C_{3-6})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-6})$ cycloalkyl $(C_{0-6})$ alkyl, phenyl $(C_{0-6})$ alkyl or hetero $(C_{5-6})$ aryl $(C_{0-6})$ alkyl and  $R^{23}$  at each occurrence independently is hydrogen or  $(C_{1-6})$ alkyl; wherein within  $R^{11}$  any alicyclic or aromatic ring system present may be substituted further by 1 to 5 radicals independently selected from  $(C_{1-6})$ alkyl,  $(C_{1-6})$ alkylidene, cyano, halo, halo-substituted  $(C_{1-4})$ alkyl, nitro,  $-X^4NR^{12}R^{12}$ ,  $-X^4NR^{12}C(O)OR^{12}$ ,  $-X^4NR^{12}C(O)NR^{12}R^{12}$ ,  $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-X^4OR^{12}$ ,  $-X^4SR^{12}$ ,  $-X^4C(O)OR^{12}$ ,  $-X^4C(O)NR^{12}R^{12}$ ,  $-X^4S(O)_2NR^{12}R^{12}$ ,  $-X^4P(O)(OR^3)OR^{12}$ ,

$-X^4OP(O)(OR^3)OR^{12}$ ,  $-X^4OC(O)R^{13}$ ,  $-X^4NR^{12}C(O)R^{13}$ ,  $-X^4S(O)R^{13}$ ,  $-X^4S(O)_2R^{13}$  and  $-X^4C(O)R^{13}$ , wherein  $X^4$ ,  $R^{12}$  and  $R^{13}$  are as defined above;

$R^2$  is hydrogen or  $(C_{1-6})$ alkyl or as defined below;

$R^3$  is hydrogen,  $(C_{1-6})$ alkyl or as defined below; and

- 5  $R^4$  is (i) hydrogen or  $(C_{1-6})$ alkyl, wherein said alkyl is optionally substituted with cyano, halo, nitro,  $-NR^{12}R^{12}$ ,  $-NR^{12}C(O)OR^{12}$ ,  $-NR^{12}C(O)NR^{12}R^{12}$ ,  $-NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-OR^{12}$ ,  $-SR^{12}$ ,  $-C(O)OR^{12}$ ,  $-C(O)NR^{12}R^{12}$ ,  $-S(O)_2NR^{12}R^{12}$ ,  $-P(O)(OR^{12})OR^{12}$ ,  $-OP(O)(OR^{12})OR^{12}$ ,  $-NR^{12}C(O)R^{13}$ ,  $-S(O)R^{13}$ ,  $-S(O)_2R^{13}$ ,  $-C(O)R^{13}$ ,  $-OR^{14}$ ,  $-SR^{14}$ ,  $-S(O)R^{14}$ ,  $-S(O)_2R^{14}$ ,  $-C(O)R^{14}$ ,  $-C(O)OR^{14}$ ,  $-OC(O)R^{14}$ ,  $-NR^{14}R^{15}$ ,  $-NR^{15}C(O)R^{14}$ ,  $-NR^{15}C(O)OR^{14}$ ,  $-C(O)NR^{14}R^{15}$ ,  $-S(O)_2NR^{14}R^{15}$ ,  $-NR^{15}C(O)NR^{14}R^{15}$  or  $-NR^{15}C(NR^{15})NR^{14}R^{15}$ , wherein  $R^{12}$ ,  $R^{13}$ ,  $R^{14}$  and  $R^{15}$  are as defined above, or (ii) a group selected from  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  $(C_{9-12})$ polycycloaryl $(C_{0-6})$ alkyl and hetero $(C_{8-12})$ polycycloaryl $(C_{0-6})$ alkyl, wherein said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a group selected from  $-R^{16}$ ,  $-X^4OR^{16}$ ,  $-X^4SR^{16}$ ,  $-X^4S(O)R^{16}$ ,  $-X^4S(O)_2R^{16}$ ,  $-X^4C(O)R^{16}$ ,  $-X^4C(O)OR^{16}$ ,  $-X^4OC(O)R^{16}$ ,  $-X^4NR^{16}R^{17}$ ,  $-X^4NR^{17}C(O)R^{16}$ ,  $-X^4NR^{17}C(O)OR^{16}$ ,  $-X^4C(O)NR^{16}R^{17}$ ,  $-X^4S(O)_2NR^{16}R^{17}$ ,  $-X^4NR^{17}C(O)NR^{16}R^{17}$  or  $-X^4NR^{17}C(NR^{17})NR^{16}R^{17}$ , wherein  $X^4$ ,  $R^{16}$  and  $R^{17}$  are as defined above; wherein within  $R^9$  and/or  $R^{10}$  any alicyclic or aromatic ring system present may be substituted further by 1 to 5 radicals independently selected from  $(C_{1-6})$ alkyl,  $(C_{1-6})$ alkylidene, cyano, halo, halo-substituted  $(C_{1-4})$ alkyl, nitro,  $-X^4NR^{12}R^{12}$ ,  $-X^4NR^{12}C(O)OR^{12}$ ,  $-X^4NR^{12}C(O)NR^{12}R^{12}$ ,  $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-X^4OR^{12}$ ,  $-X^4SR^{12}$ ,  $-X^4C(O)OR^{12}$ ,  $-X^4C(O)NR^{12}R^{12}$ ,  $-X^4S(O)_2NR^{12}R^{12}$ ,  $-X^4P(O)(OR^3)OR^{12}$ ,  $-X^4OP(O)(OR^3)OR^{12}$ ,  $-X^4OC(O)R^{13}$ ,  $-X^4NR^{12}C(O)R^{13}$ ,  $-X^4S(O)R^{13}$ ,  $-X^4S(O)_2R^{13}$  and  $-X^4C(O)R^{13}$ , wherein  $X^4$ ,  $R^{12}$  and  $R^{13}$  are as defined above, or

$R^4$  and  $R^2$  taken together form trimethylene, tetramethylene or phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene, or

$R^4$  and  $R^3$  together with the carbon atom to which both  $R^4$  and  $R^3$  are attached form  $(C_{3-8})$ cycloalkylene or  $(C_{3-8})$ heterocycloalkylene; and the *N*-oxide derivatives, prodrug

derivatives, protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable salts thereof.

2. The compound of Claim 1 in which:

R<sup>1</sup> is a group of Formula (a) wherein within Formula (a):

X<sup>1</sup> is -C(O)-;

R<sup>5</sup> is hydrogen or (C<sub>1-6</sub>)alkyl;

R<sup>7</sup> is hydrogen or methyl;

R<sup>9</sup> is (i) (C<sub>1-6</sub>)alkyl optionally substituted with -OR<sup>14</sup>, -SR<sup>14</sup>, -S(O)R<sup>14</sup>, -S(O)<sub>2</sub>R<sup>14</sup>, -C(O)R<sup>14</sup>, -C(O)OR<sup>14</sup>, -OC(O)R<sup>14</sup>, -NR<sup>14</sup>R<sup>15</sup>, -NR<sup>15</sup>C(O)R<sup>14</sup>, -NR<sup>15</sup>C(O)OR<sup>14</sup>, -C(O)NR<sup>14</sup>R<sup>15</sup>, -S(O)<sub>2</sub>NR<sup>14</sup>R<sup>15</sup>, -NR<sup>15</sup>C(O)NR<sup>14</sup>R<sup>15</sup> or -NR<sup>15</sup>C(NR<sup>15</sup>)NR<sup>14</sup>R<sup>15</sup>, wherein R<sup>14</sup> is (C<sub>3-10</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-10</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-10</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-10</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-10</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>8-10</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl and R<sup>15</sup> is hydrogen or (C<sub>1-6</sub>)alkyl, and wherein within R<sup>14</sup> said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a group selected from -R<sup>16</sup>, -X<sup>3</sup>OR<sup>16</sup>, -X<sup>3</sup>SR<sup>16</sup>, -X<sup>3</sup>S(O)R<sup>16</sup>, -X<sup>3</sup>S(O)<sub>2</sub>R<sup>16</sup>, -X<sup>3</sup>C(O)R<sup>16</sup>, -X<sup>3</sup>C(O)OR<sup>16</sup>, -X<sup>3</sup>OC(O)R<sup>16</sup>, -X<sup>3</sup>NR<sup>16</sup>R<sup>17</sup>, -X<sup>3</sup>NR<sup>17</sup>C(O)R<sup>16</sup>, -X<sup>3</sup>NR<sup>17</sup>C(O)OR<sup>16</sup>, -X<sup>3</sup>C(O)NR<sup>16</sup>R<sup>17</sup>, -X<sup>3</sup>S(O)<sub>2</sub>NR<sup>16</sup>R<sup>17</sup>, -X<sup>3</sup>NR<sup>17</sup>C(O)NR<sup>16</sup>R<sup>17</sup> or -X<sup>3</sup>NR<sup>17</sup>C(NR<sup>17</sup>)NR<sup>16</sup>R<sup>17</sup>, wherein X<sup>3</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>16</sup> is hydrogen or (C<sub>1-6</sub>)alkyl and R<sup>17</sup> is (C<sub>3-10</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-10</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-10</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-10</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-10</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>8-10</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl, or (ii) a group selected from (C<sub>3-10</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-10</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-10</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-10</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-10</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl and hetero(C<sub>8-10</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl, wherein said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a group selected from -R<sup>16</sup>, -X<sup>3</sup>OR<sup>16</sup>, -X<sup>3</sup>SR<sup>16</sup>, -X<sup>3</sup>S(O)R<sup>16</sup>, -X<sup>3</sup>S(O)<sub>2</sub>R<sup>16</sup>, -X<sup>3</sup>C(O)R<sup>16</sup>, -X<sup>3</sup>C(O)OR<sup>16</sup>, -X<sup>3</sup>OC(O)R<sup>16</sup>, -X<sup>3</sup>NR<sup>16</sup>R<sup>17</sup>, -X<sup>3</sup>NR<sup>17</sup>C(O)R<sup>16</sup>,

-X<sup>3</sup>NR<sup>17</sup>C(O)OR<sup>16</sup>, -X<sup>3</sup>C(O)NR<sup>16</sup>R<sup>17</sup>, -X<sup>3</sup>S(O)<sub>2</sub>NR<sup>16</sup>R<sup>17</sup>, -X<sup>3</sup>NR<sup>17</sup>C(O)NR<sup>16</sup>R<sup>17</sup> or  
 -X<sup>3</sup>NR<sup>17</sup>C(NR<sup>17</sup>)NR<sup>16</sup>R<sup>17</sup>, wherein X<sup>3</sup>, R<sup>16</sup> and R<sup>17</sup> are as defined above; wherein  
 within R<sup>9</sup> any alicyclic or aromatic ring system present may be substituted further by 1  
 to 5 radicals independently selected from (C<sub>1-6</sub>)alkyl, (C<sub>1-6</sub>)alkylidene, cyano, halo,  
 5 halo-substituted (C<sub>1-4</sub>)alkyl, nitro, -X<sup>3</sup>NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>,  
 -X<sup>3</sup>NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>OR<sup>12</sup>, -X<sup>3</sup>SR<sup>12</sup>,  
 -X<sup>3</sup>C(O)OR<sup>12</sup>, -X<sup>3</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>P(O)(OR<sup>3</sup>)OR<sup>12</sup>,  
 -X<sup>3</sup>OP(O)(OR<sup>3</sup>)OR<sup>12</sup>, -X<sup>3</sup>OC(O)R<sup>13</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)R<sup>13</sup>, -X<sup>3</sup>S(O)R<sup>13</sup>, -X<sup>3</sup>S(O)<sub>2</sub>R<sup>13</sup>  
 and -X<sup>3</sup>C(O)R<sup>13</sup>, wherein X<sup>3</sup> is as defined above, R<sup>12</sup> at each occurrence  
 10 independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl and R<sup>13</sup> is  
 (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl; and

R<sup>11</sup> is -X<sup>4</sup>X<sup>5</sup>R<sup>18</sup>, wherein X<sup>4</sup> is -C(O)- or -S(O)<sub>2</sub>-, X<sup>5</sup> is a bond, -O- or  
 -NR<sup>19</sup>-, wherein R<sup>19</sup> is hydrogen or (C<sub>1-6</sub>)alkyl, and R<sup>18</sup> is (i) (C<sub>1-10</sub>)alkyl or  
 (ii) (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl,  
 15 (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl or (iii) (C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl,  
 hetero(C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, phenyl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl,  
 wherein said cycloalkyl, heterocycloalkyl, phenyl or heteroaryl is substituted by  
 -X<sup>9</sup>OR<sup>24</sup>, -X<sup>9</sup>C(O)R<sup>24</sup>, -X<sup>9</sup>C(O)OR<sup>24</sup>, -X<sup>9</sup>C(O)NR<sup>24</sup>R<sup>25</sup>, -X<sup>9</sup>NR<sup>24</sup>R<sup>25</sup>,  
 -X<sup>9</sup>NR<sup>25</sup>C(O)R<sup>24</sup>, -X<sup>9</sup>NR<sup>25</sup>C(O)OR<sup>24</sup>, -X<sup>9</sup>NR<sup>25</sup>C(O)NR<sup>24</sup>R<sup>25</sup> or  
 20 -X<sup>9</sup>NR<sup>25</sup>C(NR<sup>25</sup>)NR<sup>24</sup>R<sup>25</sup>, wherein X<sup>9</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>24</sup> is  
 (C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, phenyl(C<sub>0-6</sub>)alkyl or  
 hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl and R<sup>25</sup> is hydrogen or (C<sub>1-6</sub>)alkyl, wherein within R<sup>11</sup> any  
 alicyclic or aromatic ring system present may be substituted further by 1 to 5  
 substituents independently selected from (C<sub>1-6</sub>)alkyl, halo, halo-substituted (C<sub>1-4</sub>)alkyl,  
 25 -OR<sup>12</sup>, -X<sup>3</sup>SR<sup>12</sup>, -C(O)OR<sup>12</sup> and -X<sup>3</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>, wherein X<sup>3</sup> is a bond or  
 (C<sub>1-6</sub>)alkylene and R<sup>14</sup> is hydrogen or (C<sub>1-6</sub>)alkyl;

R<sup>2</sup> is hydrogen;

R<sup>3</sup> is hydrogen or (C<sub>1-4</sub>)alkyl or taken with R<sup>4</sup> together with the carbon atom to which  
 both R<sup>3</sup> and R<sup>4</sup> are attached forms (C<sub>3-8</sub>)cycloalkylene; and

R<sup>4</sup> is hydrogen or as defined above; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable salts thereof.

3. The compound of Claim 2 in which:

5 R<sup>1</sup> is a group of Formula (a) wherein within Formula (a):

R<sup>5</sup> and R<sup>7</sup> both are hydrogen;

R<sup>9</sup> is (i) (C<sub>1-6</sub>)alkyl optionally substituted with -OR<sup>14</sup> or -SR<sup>14</sup>, wherein R<sup>14</sup> is (C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, phenyl(C<sub>0-6</sub>)alkyl, biphenyl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl, or (ii) a group selected from (C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, phenyl(C<sub>0-6</sub>)alkyl, biphenyl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-10</sub>)aryl(C<sub>0-6</sub>)alkyl; wherein within 10 R<sup>9</sup> any alicyclic or aromatic ring system present may be substituted further by 1 to 5 radicals independently selected from (C<sub>1-6</sub>)alkyl, (C<sub>1-6</sub>)alkylidene, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro, -X<sup>3</sup>NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>OR<sup>12</sup>, -X<sup>3</sup>SR<sup>12</sup>, -X<sup>3</sup>C(O)OR<sup>12</sup>, -X<sup>3</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>P(O)(OR<sup>3</sup>)OR<sup>12</sup>, -X<sup>3</sup>OP(O)(OR<sup>3</sup>)OR<sup>12</sup>, -X<sup>3</sup>OC(O)R<sup>13</sup>, -X<sup>3</sup>OC(O)R<sup>13</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)R<sup>13</sup>, -X<sup>3</sup>S(O)R<sup>13</sup>, -X<sup>3</sup>S(O)<sub>2</sub>R<sup>13</sup> and -X<sup>3</sup>C(O)R<sup>13</sup>, wherein X<sup>3</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>12</sup> at each occurrence independently is hydrogen, (C<sub>1-3</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl and R<sup>13</sup> is (C<sub>1-3</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl; and

20 R<sup>11</sup> is -X<sup>4</sup>X<sup>5</sup>R<sup>18</sup>, wherein X<sup>4</sup> is -C(O)-, X<sup>5</sup> is a bond and R<sup>18</sup> is

(i) (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl or (ii) phenyl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl, wherein said phenyl or heteroaryl is substituted by -X<sup>9</sup>OR<sup>24</sup>, -X<sup>9</sup>C(O)R<sup>24</sup>, -X<sup>9</sup>C(O)OR<sup>24</sup>, -X<sup>9</sup>C(O)NR<sup>24</sup>R<sup>25</sup>, -X<sup>9</sup>NR<sup>24</sup>R<sup>25</sup>, -X<sup>9</sup>NR<sup>25</sup>C(O)R<sup>24</sup>, -X<sup>9</sup>NR<sup>25</sup>C(O)OR<sup>24</sup>, -X<sup>9</sup>NR<sup>25</sup>C(O)NR<sup>24</sup>R<sup>25</sup> or -X<sup>9</sup>NR<sup>25</sup>C(NR<sup>25</sup>)NR<sup>24</sup>R<sup>25</sup>, wherein X<sup>9</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>24</sup> is phenyl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl and R<sup>25</sup> is hydrogen or (C<sub>1-6</sub>)alkyl, 25 wherein within R<sup>11</sup> any aromatic ring system present may be substituted further by 1 to



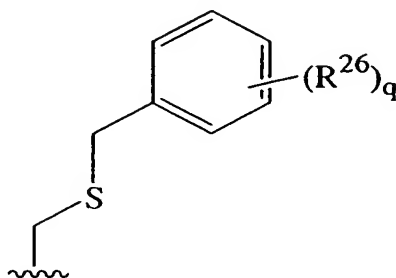
5 substituents independently selected from (C<sub>1-6</sub>)alkyl, halo, halo-substituted (C<sub>1-4</sub>)alkyl, -OR<sup>12</sup>, -X<sup>3</sup>SR<sup>12</sup>, -C(O)OR<sup>12</sup> and -X<sup>3</sup>NR<sup>12</sup>C(O)OR<sup>12</sup> wherein X<sup>3</sup> is a bond or (C<sub>1-6</sub>)alkylene and R<sup>12</sup> is hydrogen or (C<sub>1-6</sub>)alkyl; and

R<sup>3</sup> and R<sup>4</sup> are both hydrogen; and the *N*-oxide derivatives, prodrug derivatives,

- 5 protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable salts thereof; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable salts thereof.

4. The compound of Claim 3 in which within Formula (a) R<sup>9</sup> is cyclohexylmethyl,  
 10 wherein said cyclohexyl may be substituted by 1 to 5 radicals independently selected from (C<sub>1-4</sub>)alkyl, (C<sub>1-6</sub>)alkylidene or -X<sup>3</sup>OC(O)R<sup>13</sup>, or phenylmethylsulfanylmethyl or phenylsulfanylethyl, wherein said phenyl may be substituted by 1 to 5 radicals independently selected from (C<sub>1-4</sub>)alkyl, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro, -OR<sup>12</sup>, -SR<sup>12</sup> and -C(O)OR<sup>12</sup>, wherein R<sup>12</sup> is hydrogen, (C<sub>1-3</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl and R<sup>13</sup> is  
 15 (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl; and R<sup>11</sup> is benzoyl, furylcarbonyl, phenyloxybenzoyl, pyridylthienylcarbonyl, benzoylbenzoyl, thienylcarbonyl, morpholinylcarbonyl, phenyluriedobenzoyl, cyclohexenylcarbonyl or piperazinylcarbonyl, wherein within R<sup>11</sup> any aromatic ring system present may be substituted further by 1 to 2 substituents independently selected from (C<sub>1-6</sub>)alkyl, *tert*-butoxycarbonylamino,  
 20 *tert*-butoxycarbonylaminomethyl, bromo, chloro, ethoxy, fluoro, hydroxy, methoxy and methylsulfanyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable salts thereof.

5. The compound of Claim 4 in which within Formula (a),  $R^9$  is a group having the following formula:



in which  $q$  is 0 to 5 and  $R^{26}$  at each occurrence is independently selected from  $(C_{1-4})$ alkyl, cyano, halo, halo-substituted  $(C_{1-4})$ alkyl, nitro,  $-OR^{12}$ ,  $-SR^{12}$  and  $-C(O)OR^{12}$ , wherein  $R^{12}$  is hydrogen,  $(C_{1-3})$ alkyl or halo-substituted  $(C_{1-3})$ alkyl and  $R^{13}$  is  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-3})$ alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable salts thereof.

6. The compound of Claim 3 in which within Formula (a),  $R^9$  is
- 10 benzylsulfanylmethyl, 2-bromobenzylsulfanylmethyl, 2-chlorobenzylsulfanyl, 2-(2-chlorophenylsulfanyl)ethyl, cyclohexyl, 4-ethylidenecyclohexyl, 2-iodobenzylsulfanylmethyl, 2-methylbenzylsulfanylmethyl, 3-methyl-3-trifluorocarbonyloxycyclohexylmethyl, 4-methylenecyclohexylmethyl or 2-nitrobenzylsulfanylmethyl and  $R^{11}$  is 4-*tert*-butoxycarbonylaminobenzoyl,
- 15 3-*tert*-butoxycarbonylaminomethylbenzoyl, 2-(3,5-dimethoxyphenyl)thiazol-4-ylcarbonyl, fur-3-ylcarbonyl, 4-methoxybenzoyl, 3-methylbenzoyl, 3-phenoxybenzoyl, 5-pyrid-2-ylthien-2-ylcarbonyl, 3-benzoylbenzoyl, 4-methylbenzoyl, thien-2-ylcarbonyl, morpholin-4-ylcarbonyl, 5-bromothien-2-ylcarbonyl, 5-chlorothien-2-ylcarbonyl, 5-methylthien-2-ylcarbonyl, 2-(2-chloro-6-methylphenyl)ureidobenzoyl, cyclohexyl-1-en-1-ylcarbonyl, 3-ethoxybenzoyl, 3-fluorobenzoyl, 4-fluorobenzoyl and piperidin-1-ylcarbonyl;
- 20 and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and

mixtures of isomers; and the pharmaceutically acceptable salts thereof.

7. The compound of Claim 6 selected from a group consisting of:

*N*-(2-benzylsulfanyl-1*R*-cyanomethylcarbamoyl-ethyl)-4-hydroxybenzamide;

*N*-[2-(2-bromobenzylsulfanyl)-1*R*-cyanomethylcarbamoyl-ethyl]benzamide;

5 *N*-[1*R*-cyanomethylcarbamoyl-2-(2-iodobenzylsulfanyl)ethyl]benzamide;

*N*-[1*R*-cyanomethylcarbamoyl-2-(2-cyanobenzylsulfanyl)ethyl]morpholine-4-carboxamide;

*N*-[3-(2-chlorophenylsulfanyl)-1*R*-cyanomethylcarbamoylpropyl]benzamide;

*N*-[1*R*-cyanomethylcarbamoyl-2-(2-nitrobenzylsulfanyl)ethyl]morpholine-

10 4-carboxamide

*N*-[1*R*-cyanomethylcarbamoyl-2-(2-methylbenzylsulfanyl)ethyl]morpholine-4-carboxamide; and

*N*-[1*R*-cyanomethylcarbamoyl-2-(2-methylbenzylsulfanyl)ethyl]benzamide; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and

15 mixtures of isomers; and the pharmaceutically acceptable salts thereof.

8. A pharmaceutical composition comprising a compound of Claim 1, or a *N*-oxide derivative, prodrug derivative, individual isomer, mixture of isomers, or a pharmaceutically acceptable salt thereof in admixture with one or more suitable excipients.

9. A method of treating a disease in an animal in which cysteine protease activity  
20 contributes to the pathology and/or symptomatology of the disease, which method comprises administering to the animal a therapeutically effective amount of compound of Claim 1; or a *N*-oxide derivative, prodrug derivative, individual isomer or mixture of isomers or a pharmaceutically acceptable salt thereof.

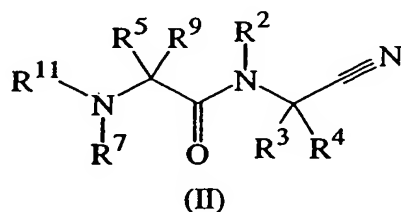
10. The method of Claim 9 in which the cysteine protease is cathepsin S.

11. The method of Claim 10 in which the disease is an autoimmune disorder, allergic disorder, allogeneic immune response, a disorder involving excessive elastolysis, cardiovascular disorders or a disorder involving fibril formation.

12. The method of Claim 11 in which the disorder is selected from juvenile onset diabetes, multiple sclerosis, pemphigus vulgaris, Graves' disease, myasthenia gravis, systemic lupus erythematosus, rheumatoid arthritis, Hashimoto's thyroiditis, asthma, organ transplant or tissue graft rejections, chronic obstructive pulmonary disease, bronchiolitis, excessive airway elastolysis in asthma and bronchitis, pneumonitis, plaque rupture, atheroma and systemic amyloidosis.

13. A compound according to claim 1 in which  $R^1$  is a group of formula (a) wherein  $X^1$  is  $-\text{CH}_2\text{S}(\text{O})_2-$ ; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable salts thereof.

14. A compound of Formula (II):



wherein:

$R^2$  is hydrogen or  $(\text{C}_{1-6})$ alkyl or as defined below;

$R^3$  is hydrogen,  $(\text{C}_{1-6})$ alkyl or as defined below;

20  $R^4$  is (i) hydrogen or  $(\text{C}_{1-6})$ alkyl, wherein said alkyl optionally is substituted with cyano, halo, nitro,  $-\text{NR}^{12}\text{R}^{12}$ ,  $-\text{NR}^{12}\text{C}(\text{O})\text{OR}^{12}$ ,  $-\text{NR}^{12}\text{C}(\text{O})\text{NR}^{12}\text{R}^{12}$ ,  $-\text{NR}^{12}\text{C}(\text{NR}^{12})\text{NR}^{12}\text{R}^{12}$ ,  $-\text{OR}^{12}$ ,  $-\text{SR}^{12}$ ,  $-\text{C}(\text{O})\text{OR}^{12}$ ,  $-\text{C}(\text{O})\text{NR}^{12}\text{R}^{12}$ ,  $-\text{S}(\text{O})_2\text{NR}^{12}\text{R}^{12}$ ,

- P(O)(OR<sup>12</sup>)OR<sup>12</sup>, -OP(O)(OR<sup>12</sup>)OR<sup>12</sup>, -NR<sup>12</sup>C(O)R<sup>13</sup>, -S(O)R<sup>13</sup>, -S(O)<sub>2</sub>R<sup>13</sup>, -C(O)R<sup>13</sup>, -OR<sup>14</sup>, -SR<sup>14</sup>, -S(O)R<sup>14</sup>, -S(O)<sub>2</sub>R<sup>14</sup>, -C(O)R<sup>14</sup>, -C(O)OR<sup>14</sup>, -OC(O)R<sup>14</sup>, -NR<sup>14</sup>R<sup>15</sup>, -NR<sup>15</sup>C(O)R<sup>14</sup>, -NR<sup>15</sup>C(O)OR<sup>14</sup>, -C(O)NR<sup>14</sup>R<sup>15</sup>, -S(O)<sub>2</sub>NR<sup>14</sup>R<sup>15</sup>, -NR<sup>15</sup>C(O)NR<sup>14</sup>R<sup>15</sup> or -NR<sup>15</sup>C(NR<sup>15</sup>)NR<sup>14</sup>R<sup>15</sup>, wherein R<sup>12</sup> at each occurrence independently is hydrogen,
- 5 (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl; R<sup>13</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl, R<sup>14</sup> is (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>8-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl and R<sup>15</sup> is hydrogen or (C<sub>1-6</sub>)alkyl, and wherein within R<sup>14</sup> said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, polycycloaryl or heteropolycycloaryl ring
- 10 optionally is substituted by a group selected from -R<sup>16</sup>, -X<sup>4</sup>OR<sup>16</sup>, -X<sup>4</sup>SR<sup>16</sup>, -X<sup>4</sup>S(O)R<sup>16</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>16</sup>, -X<sup>4</sup>C(O)R<sup>16</sup>, -X<sup>4</sup>C(O)OR<sup>16</sup>, -X<sup>4</sup>OC(O)R<sup>16</sup>, -X<sup>4</sup>NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)R<sup>16</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)OR<sup>16</sup>, -X<sup>4</sup>C(O)NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>S(O)<sub>2</sub>NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)NR<sup>16</sup>R<sup>17</sup> or -X<sup>4</sup>NR<sup>17</sup>C(NR<sup>17</sup>)NR<sup>16</sup>R<sup>17</sup>, wherein X<sup>4</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>16</sup> is hydrogen or (C<sub>1-6</sub>)alkyl and R<sup>17</sup> is (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl,
- 15 (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>8-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl, or (ii) a group selected from (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl and hetero(C<sub>8-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl, wherein said cycloalkyl, heterocycloalkyl, aryl,
- 20 heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a group selected from -R<sup>16</sup>, -X<sup>4</sup>OR<sup>16</sup>, -X<sup>4</sup>SR<sup>16</sup>, -X<sup>4</sup>S(O)R<sup>16</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>16</sup>, -X<sup>4</sup>C(O)R<sup>16</sup>, -X<sup>4</sup>C(O)OR<sup>16</sup>, -X<sup>4</sup>OC(O)R<sup>16</sup>, -X<sup>4</sup>NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)R<sup>16</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)OR<sup>16</sup>, -X<sup>4</sup>C(O)NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>S(O)<sub>2</sub>NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)NR<sup>16</sup>R<sup>17</sup> or -X<sup>4</sup>NR<sup>17</sup>C(NR<sup>17</sup>)NR<sup>16</sup>R<sup>17</sup>, wherein X<sup>4</sup>, R<sup>16</sup> and R<sup>17</sup> are as defined above; wherein within R<sup>4</sup> any alicyclic or aromatic ring
- 25 system present may be substituted further by 1 to 5 radicals independently selected from (C<sub>1-6</sub>)alkyl, (C<sub>1-6</sub>)alkylidene, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro, -X<sup>4</sup>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>OR<sup>12</sup>, -X<sup>4</sup>SR<sup>12</sup>, -X<sup>4</sup>C(O)OR<sup>12</sup>, -X<sup>4</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>P(O)(OR<sup>3</sup>)OR<sup>12</sup>, -X<sup>4</sup>OP(O)(OR<sup>3</sup>)OR<sup>12</sup>, -X<sup>4</sup>OC(O)R<sup>13</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)R<sup>13</sup>, -X<sup>4</sup>S(O)R<sup>13</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>13</sup> and

$-X^4\dot{C}(O)R^{13}$ , wherein  $X^4$ ,  $R^{12}$  and  $R^{13}$  are as defined above, or

$R^4$  and  $R^2$  taken together form trimethylene, tetramethylene or phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene, or

$R^4$  and  $R^3$  together with the carbon atom to which both  $R^4$  and  $R^3$  are attached form

5 (C<sub>3-8</sub>)cycloalkylene or (C<sub>3-8</sub>)heterocycloalkylene;

$R^5$  is hydrogen or (C<sub>1-6</sub>)alkyl;

$R^7$  is hydrogen or (C<sub>1-6</sub>)alkyl;

$R^9$  is (C<sub>6-12</sub>)aryl(C<sub>1-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>1-6</sub>)alkyl,  $-X^4OR^{14}$ ,  $-X^4SR^{14}$ ,  $-X^4S(O)R^{14}$ ,  $-X^4S(O)_2R^{14}$  or  $-X^4NR^{14}R^{15}$ , wherein  $X^4$ ,  $R^{14}$  and  $R^{15}$  are as defined above and

10 wherein within  $R^9$  said aryl or heteroaryl ring optionally is substituted by 1 to 5 radicals independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro,

$-X^4NR^{12}R^{12}$ ,  $-X^4NR^{12}C(O)OR^{12}$ ,  $-X^4NR^{12}C(O)NR^{12}R^{12}$ ,  $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-X^4OR^{12}$ ,  $-X^4SR^{12}$ ,  $-X^4C(O)R^{12}$ ,  $-X^4C(O)OR^{12}$ ,  $-X^4C(O)NR^{12}R^{12}$ ,  $-X^4S(O)_2NR^{12}R^{12}$ ,  $-X^4P(O)(OR^3)OR^{12}$ ,  $-X^4OP(O)(OR^3)OR^{12}$ ,  $-X^4OC(O)R^{13}$ ,  $-X^4NR^{12}C(O)R^{13}$ ,  $-X^4S(O)R^{13}$ ,

15  $-X^4S(O)_2R^{13}$ , wherein  $X^4$ ,  $R^{12}$  and  $R^{13}$  are as defined above; and

$R^{11}$  is  $-X^5X^6R^{18}$ , wherein  $X^5$  is  $-C(O)-$ ,  $-C(O)C(O)-$  or  $-S(O)_2-$ ,  $X^6$  is a bond,  $-O-$  or  $-NR^{19}-$ , wherein  $R^{19}$  is hydrogen or (C<sub>1-6</sub>)alkyl, and  $R^{18}$  is (i) (C<sub>1-10</sub>)alkyl optionally substituted by cyano, halo, nitro,  $-NR^{12}R^{12}$ ,  $-NR^{12}C(O)OR^{12}$ ,  $-NR^{12}C(O)NR^{12}R^{12}$ ,  $-NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-OR^{12}$ ,  $-SR^{12}$ ,  $-C(O)OR^{12}$ ,  $-C(O)NR^{12}R^{12}$ ,  $-S(O)_2NR^{12}R^{12}$ ,

20  $-P(O)(OR^{12})OR^{12}$ ,  $-OP(O)(OR^{12})OR^{12}$ ,  $-NR^{12}C(O)R^{13}$ ,  $-S(O)R^{13}$ ,  $-S(O)_2R^{13}$ ,  $-C(O)R^{13}$ ,  $-OR^{20}$ ,  $-SR^{20}$ ,  $-S(O)R^{20}$ ,  $-S(O)_2R^{20}$ ,  $-C(O)R^{20}$ ,  $-C(O)OR^{20}$ ,  $-C(O)NR^{20}R^{21}$ ,  $-NR^{20}R^{21}$ ,  $-NR^{21}C(O)R^{20}$ ,  $-NR^{21}C(O)OR^{20}$ ,  $-NR^{21}C(O)NR^{20}R^{21}$  or  $-NR^{21}C(NR^{21})NR^{20}R^{21}$ , wherein

$R^{12}$  and  $R^{13}$  are as defined above,  $R^{20}$  is (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl,

hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl,

25 (C<sub>9-12</sub>)bicycloaryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>8-12</sub>)bicycloaryl(C<sub>0-6</sub>)alkyl and  $R^{21}$  at each occurrence independently is hydrogen or (C<sub>1-6</sub>)alkyl, or (ii) (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl,

hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl,

(C<sub>9-12</sub>)bicycloaryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>8-12</sub>)bicycloaryl(C<sub>0-6</sub>)alkyl or

(iii) (C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, phenyl(C<sub>0-6</sub>)alkyl or

- hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl, wherein said cycloalkyl, heterocycloalkyl, phenyl or heteroaryl is substituted by -X<sup>4</sup>OR<sup>22</sup>, -X<sup>4</sup>SR<sup>22</sup>, -X<sup>4</sup>S(O)R<sup>22</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>22</sup>, -X<sup>4</sup>C(O)R<sup>22</sup>, -X<sup>4</sup>C(O)OR<sup>22</sup>, -X<sup>4</sup>C(O)NR<sup>22</sup>R<sup>23</sup>, -X<sup>4</sup>NR<sup>22</sup>R<sup>23</sup>, -X<sup>4</sup>NR<sup>23</sup>C(O)R<sup>22</sup>, -X<sup>4</sup>NR<sup>23</sup>C(O)OR<sup>22</sup>, -X<sup>4</sup>NR<sup>23</sup>C(O)NR<sup>22</sup>R<sup>23</sup> or -X<sup>4</sup>NR<sup>23</sup>C(NR<sup>23</sup>)NR<sup>22</sup>R<sup>23</sup>, wherein X<sup>4</sup> is as defined above, R<sup>22</sup> is
- 5 (C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, phenyl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl and R<sup>23</sup> at each occurrence independently is hydrogen or (C<sub>1-6</sub>)alkyl; wherein within R<sup>11</sup> any alicyclic or aromatic ring system present may be substituted further by 1 to 5 radicals independently selected from (C<sub>1-6</sub>)alkyl, (C<sub>1-6</sub>)alkylidene, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro, -X<sup>4</sup>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>,
- 10 -X<sup>4</sup>NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>OR<sup>12</sup>, -X<sup>4</sup>SR<sup>12</sup>, -X<sup>4</sup>C(O)OR<sup>12</sup>, -X<sup>4</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>P(O)(OR<sup>3</sup>)OR<sup>12</sup>, -X<sup>4</sup>OP(O)(OR<sup>3</sup>)OR<sup>12</sup>, -X<sup>4</sup>OC(O)R<sup>13</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)R<sup>13</sup>, -X<sup>4</sup>S(O)R<sup>13</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>13</sup> and -X<sup>4</sup>C(O)R<sup>13</sup>, wherein X<sup>4</sup>, R<sup>12</sup> and R<sup>13</sup> are as defined above; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable
- 15 salts thereof.

15. The compound of Claim 14 in which:

R<sup>2</sup> is hydrogen;

R<sup>3</sup> is hydrogen, methyl or taken with R<sup>4</sup> together with the carbon atom to which both R<sup>3</sup> and R<sup>4</sup> are attached forms (C<sub>3-8</sub>)cycloalkylene;

20 R<sup>4</sup> is hydrogen, methyl or as defined above;

R<sup>5</sup> is hydrogen or (C<sub>1-6</sub>)alkyl;

R<sup>7</sup> is hydrogen or methyl;

R<sup>9</sup> represents (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, -X<sup>4</sup>OR<sup>14</sup>, -X<sup>4</sup>SR<sup>14</sup>, -X<sup>4</sup>S(O)R<sup>14</sup> or -X<sup>4</sup>NR<sup>14</sup>R<sup>15</sup>, wherein X<sup>4</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>14</sup> is

25 (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl and R<sup>15</sup> is hydrogen or (C<sub>1-6</sub>)alkyl, and wherein within R<sup>9</sup> said aryl or heteroaryl ring optionally is substituted by 1 to 5 radicals independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro, -X<sup>4</sup>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>OR<sup>12</sup>, -X<sup>4</sup>C(O)R<sup>12</sup>, -X<sup>4</sup>SR<sup>12</sup>, wherein X<sup>4</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>12</sup> at

each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl, and R<sup>13</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl; and

R<sup>11</sup> is -X<sup>4</sup>X<sup>5</sup>R<sup>18</sup>, wherein X<sup>4</sup> is -C(O)- or -S(O)<sub>2</sub>-, X<sup>5</sup> is a bond, -O- or -NR<sup>19</sup>-, wherein R<sup>19</sup> is hydrogen or (C<sub>1-6</sub>)alkyl, and R<sup>18</sup> is (i) (C<sub>1-10</sub>)alkyl or

- 5 (ii) (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl or (iii) (C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, phenyl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl, wherein said cycloalkyl, heterocycloalkyl, phenyl or heteroaryl is substituted by -X<sup>9</sup>OR<sup>24</sup>, -X<sup>9</sup>C(O)R<sup>24</sup>, -X<sup>9</sup>C(O)OR<sup>24</sup>, -X<sup>9</sup>C(O)NR<sup>24</sup>R<sup>25</sup>, -X<sup>9</sup>NR<sup>24</sup>R<sup>25</sup>, -X<sup>9</sup>NR<sup>25</sup>C(O)R<sup>24</sup>, -X<sup>9</sup>NR<sup>25</sup>C(O)OR<sup>24</sup>,  
10 -X<sup>9</sup>NR<sup>25</sup>C(O)NR<sup>24</sup>R<sup>25</sup> or -X<sup>9</sup>NR<sup>25</sup>C(NR<sup>25</sup>)NR<sup>24</sup>R<sup>25</sup>, wherein X<sup>9</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>24</sup> is (C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, phenyl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl and R<sup>25</sup> is hydrogen or (C<sub>1-6</sub>)alkyl, wherein within R<sup>11</sup> any alicyclic or aromatic ring system present may be substituted further by 1 to 5 substituents independently selected from (C<sub>1-6</sub>)alkyl, halo, halo-substituted (C<sub>1-4</sub>)alkyl, -OR<sup>12</sup>, -X<sup>3</sup>SR<sup>12</sup>,  
15 -C(O)OR<sup>12</sup> and -X<sup>3</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>, wherein X<sup>3</sup> is a bond or (C<sub>1-6</sub>)alkylene and R<sup>14</sup> is hydrogen or (C<sub>1-6</sub>)alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable salts thereof.

16. The compound of Claim 15 in which:

20 R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>7</sup> each are hydrogen;

R<sup>9</sup> represents benzyl, benzyloxymethyl, benzylsulfanylethyl, benzylsulfanylmethyl, benzylsulfinylmethyl, indolylmethyl, naphthylmethyl, phenethyl, phenoxyethyl, phenylamino, pyridylmethyl, pyridylsulfanylethyl, phenylsulfanylethyl, thiazolyl or thienyl, wherein within R<sup>9</sup> the aromatic ring may be substituted further by 1 to 5 radicals independently selected from  
25 (C<sub>1-6</sub>)alkyl, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro, -X<sup>4</sup>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>OR<sup>12</sup>, -X<sup>4</sup>C(O)R<sup>12</sup>, -X<sup>4</sup>SR<sup>12</sup>, wherein X<sup>4</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>12</sup> at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl, and R<sup>13</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl; and



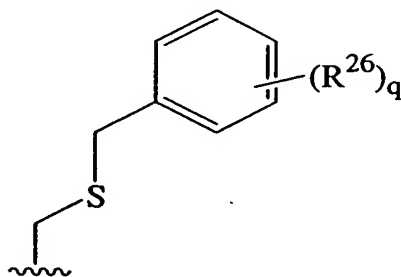
$R^{11}$  is  $-X^4X^5R^{18}$ , wherein  $X^4$  is  $-C(O)-$ ,  $X^5$  is a bond and  $R^{18}$  is

(i)  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl or hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl or (ii) phenyl $(C_{0-6})$ alkyl or hetero $(C_{5-6})$ aryl $(C_{0-6})$ alkyl, wherein said phenyl or heteroaryl is substituted by  $-X^9OR^{24}$ ,  $-X^9C(O)R^{24}$ ,  $-X^9C(O)OR^{24}$ ,

- 5  $-X^9C(O)NR^{24}R^{25}$ ,  $-X^9NR^{24}R^{25}$ ,  $-X^9NR^{25}C(O)R^{24}$ ,  $-X^9NR^{25}C(O)OR^{24}$ ,  $-X^9NR^{25}C(O)NR^{24}R^{25}$  or  $-X^9NR^{25}C(NR^{25})NR^{24}R^{25}$ , wherein  $X^9$  is a bond or  $(C_{1-6})$ alkylene,  $R^{24}$  is phenyl $(C_{0-6})$ alkyl or hetero $(C_{5-6})$ aryl $(C_{0-6})$ alkyl and  $R^{25}$  is hydrogen or  $(C_{1-6})$ alkyl, wherein within  $R^{11}$  any aromatic ring system present may be substituted further by 1 to 5 substituents independently selected from  $(C_{1-6})$ alkyl, halo, halo-substituted  $(C_{1-4})$ alkyl,  $-OR^{12}$ ,  
 10  $-X^3SR^{12}$ ,  $-C(O)OR^{12}$  and  $-X^3NR^{12}C(O)OR^{12}$  wherein  $X^3$  is a bond or  $(C_{1-6})$ alkylene and  $R^{12}$  is hydrogen or  $(C_{1-6})$ alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable salts thereof.

17. The compound of Claim 16 in which  $R^9$  is a group having the following

15 formula:



in which  $q$  is 0 to 5 and  $R^{26}$  at each occurrence is independently selected from  $(C_{1-4})$ alkyl,

cyano, halo, halo-substituted  $(C_{1-4})$ alkyl, nitro,  $-OR^{12}$ ,  $-SR^{12}$  and  $-C(O)OR^{12}$ , wherein  $R^{12}$  is

hydrogen,  $(C_{1-3})$ alkyl or halo-substituted  $(C_{1-3})$ alkyl and  $R^{13}$  is  $(C_{1-6})$ alkyl or halo-substituted

- 20  $(C_{1-3})$ alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable salts thereof.

18. The compound of Claim 17 in which R<sup>9</sup> is 4-aminobenzyl, benzyl, benzyloxymethyl, 2-benzylsulfanylethyl, benzylsulfanylmethyl, 2-bromobenzylsulfanylmethyl, 4-*tert*-butylbenzylsulfanylmethyl, 2-chlorobenzyl, 4-chlorobenzyl, 2-chlorobenzylsulfanylmethyl, 4-chlorobenzylsulfanylmethyl, 2-(2-chlorophenylsulfanyl)ethyl, 5 4-cyanobenzyl, 3,4-dichlorobenzylsulfanylmethyl, 1,6-dichlorobenzyl, 3,5-dimethylbenzylsulfanylmethyl, 2-fluorobenzyl, 4-fluorobenzyl, 2-fluorobenzylsulfanylmethyl, 1-formylindol-3-ylmethyl, indol-3-ylmethyl, 2-iodobenzylsulfanylmethyl, 2-methylbenzylsulfanylmethyl, 3-methylbenzylsulfanylmethyl, 3-methylbenzylsulfanylmethyl, 4-methylbenzylsulfanylmethyl, 2-(2-methylphenylsulfanyl)ethyl, 10 4-methoxybenzyl, 4-methoxybenzylsulfanylmethyl, 4-methoxybenzylsulfanylmethyl, naphth-2-ylmethyl, naphth-2-ylmethylsulfanylmethyl, 3-nitrobenzyl, 1-nitrobenzylsulfanylmethyl, 2-nitrobenzylsulfanylmethyl, 3-nitrobenzylsulfanylmethyl, 4-nitrobenzylsulfanylmethyl, 4-nitrobenzyl, pentafluorobenzylsulfanylmethyl, phenylamino, phenethyl, phenethyloxy, 2-phenoxyethyl, 2-phenoxyethyl 2-phenylsulfanylethyl, 15 pyrid-4-ylmethyl, pyrid-2-ylmethylsulfanylmethyl, pyrid-3-ylmethylsulfanylmethyl, pyrid-4-ylmethylsulfanylmethyl, 2-pyrid-2-ylsulfanylethyl, 2-pyrid-4-ylsulfanylethyl, thiazol-5-yl, thien-2-ylmethyl, 4-trifluoromethylbenzylsulfanylmethyl, 3-trifluoromethylbenzylsulfanylmethyl, 3-trifluoromethoxybenzylsulfanylmethyl, 4-trifluoromethoxybenzylsulfanylmethyl or 4-trifluorosulfanylbenezylsulfanylmethyl; and the 20 *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable salts thereof.

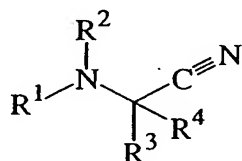
19. The compound of Claim 18 which is selected a group from consisting of:  
*N*-(2-benzylsulfanyl-1*R*-cyanomethylcarbamoylethyl)-4-hydroxybenzamide;  
*N*-[2-(2-bromobenzylsulfanyl)-1*R*-cyanomethylcarbamoylethyl]benzamide;  
 25 *N*-[1*R*-cyanomethylcarbamoyl-2-(2-iodobenzylsulfanyl)ethyl]benzamide;  
*N*-[1*R*-cyanomethylcarbamoyl-2-(2-cyanobenzylsulfanyl)ethyl]morpholine-4-carboxamide;  
*N*-[3-(2-chlorophenylsulfanyl)-1*R*-cyanomethylcarbamoylpropyl]benzamide;

*N*-[1*R*-cyanomethylcarbamoyl-2-(2-nitrobenzylsulfanyl)ethyl]morpholine-4-carboxamide

*N*-[1*R*-cyanomethylcarbamoyl-2-(2-methylbenzylsulfanyl)ethyl]morpholine-4-carboxamide; and

- 5 *N*-[1*R*-cyanomethylcarbamoyl-2-(2-methylbenzylsulfanyl)ethyl]benzamide; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers; and the pharmaceutically acceptable salts thereof.

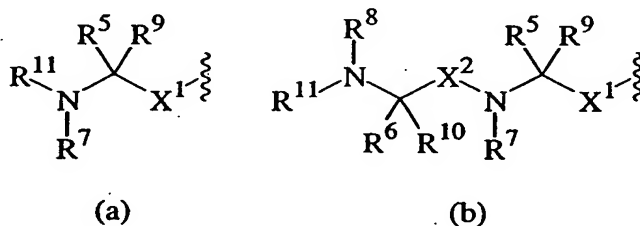
20. A method of treating a disease in an animal in which cathepsin S activity contributes to the pathology and/or symptomatology of the disease, which method comprising  
10 administering to the animal a therapeutically effective amount of a compound of Formula (I):



(I)

in which:

$\text{R}^1$  is a group of Formula (a) or (b):



- 15 wherein:

$\text{X}^1$  and  $\text{X}^2$  independently are  $-\text{C}(\text{O})-$  or  $-\text{CH}_2\text{S}(\text{O})_2-$ ;

$\text{R}^5$  and  $\text{R}^6$  are hydrogen or  $(\text{C}_{1-6})$ alkyl;

$\text{R}^7$  and  $\text{R}^8$  are hydrogen or  $(\text{C}_{1-6})$ alkyl or as defined below;

- 20  $\text{R}^9$  and  $\text{R}^{10}$  independently are (i)  $(\text{C}_{1-6})$ alkyl optionally substituted with cyano, halo or nitro or (ii) a group selected from  $-\text{X}^3\text{NR}^{12}\text{R}^{12}$ ,  $-\text{X}^3\text{NR}^{12}\text{C}(\text{O})\text{OR}^{12}$ ,

$-X^3NR^{12}C(O)NR^{12}R^{12}$ ,  $-X^3NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-X^3OR^{12}$ ,  $-X^3SR^{12}$ ,  
 $-X^3C(O)OR^{12}$ ,  $-X^3C(O)NR^{12}R^{12}$ ,  $-X^3S(O)_2NR^{12}R^{12}$ ,  $-X^3P(O)(OR^{12})OR^{12}$ ,  
 $-X^3OP(O)(OR^{12})OR^{12}$ ,  $-X^3NR^{12}C(O)R^{13}$ ,  $-X^3S(O)R^{13}$ ,  $-X^3S(O)_2R^{13}$ ,  $-X^3C(O)R^{13}$ ,  
 $-X^3C(O)R^{14}$ ,  $-X^3C(O)OR^{14}$ ,  $-X^3OC(O)R^{14}$ ,  $-X^3NR^{15}C(O)R^{14}$ ,  $-X^3NR^{15}C(O)OR^{14}$ ,  
5  $-X^3C(O)NR^{14}R^{15}$ ,  $-X^3S(O)_2NR^{14}R^{15}$ ,  $-X^3NR^{15}C(O)NR^{14}R^{15}$ ,  
 $-X^3NR^{15}C(NR^{15})NR^{14}R^{15}$ ,  $-X^4SR^{14}$ ,  $-X^4S(O)R^{14}$ ,  $-X^4S(O)_2R^{14}$ ,  $-X^4OR^{14}$ , or  
 $-X^4NR^{14}R^{15}$ , wherein  $X^3$  is  $(C_{1-6})$ alkylene,  $X^4$  is a bond or  $(C_{1-6})$ alkylene,  $R^{12}$  at each  
occurrence independently is hydrogen,  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-3})$ alkyl,  $R^{13}$   
is  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-3})$ alkyl,  $R^{14}$  is  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  
10 hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  
 $(C_{9-12})$ polycycloaryl $(C_{0-6})$ alkyl or hetero $(C_{8-12})$ polycycloaryl $(C_{0-6})$ alkyl and  $R^{15}$  is  
hydrogen or  $(C_{1-6})$ alkyl, and wherein within  $R^{14}$  said cycloalkyl, heterocycloalkyl, aryl,  
heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a  
group selected from  $-R^{16}$ ,  $-X^4OR^{16}$ ,  $-X^4SR^{16}$ ,  $-X^4S(O)R^{16}$ ,  $-X^4S(O)_2R^{16}$ ,  
15  $-X^4C(O)R^{16}$ ,  $-X^4C(O)OR^{16}$ ,  $-X^4OC(O)R^{16}$ ,  $-X^4NR^{16}R^{17}$ ,  $-X^4NR^{17}C(O)R^{16}$ ,  
 $-X^4NR^{17}C(O)OR^{16}$ ,  $-X^4C(O)NR^{16}R^{17}$ ,  $-X^4S(O)_2NR^{16}R^{17}$ ,  $-X^4NR^{17}C(O)NR^{16}R^{17}$  or  
 $-X^4NR^{17}C(NR^{17})NR^{16}R^{17}$ , wherein  $X^4$  is a bond or  $(C_{1-6})$ alkylene,  $R^{16}$  is hydrogen or  
 $(C_{1-6})$ alkyl and  $R^{17}$  is  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  
 $(C_{6-12})$ aryl $(C_{0-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  $(C_{9-12})$ polycycloaryl $(C_{0-6})$ alkyl or  
20 hetero $(C_{8-12})$ polycycloaryl $(C_{0-6})$ alkyl, or (iii) a group selected from  
 $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl,  
hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  $(C_{9-12})$ polycycloaryl $(C_{0-6})$ alkyl and  
hetero $(C_{8-12})$ polycycloaryl $(C_{0-6})$ alkyl, wherein said cycloalkyl, heterocycloalkyl, aryl,  
heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a  
25 group selected from  $-R^{16}$ ,  $-X^4OR^{16}$ ,  $-X^4SR^{16}$ ,  $-X^4S(O)R^{16}$ ,  $-X^4S(O)_2R^{16}$ ,  
 $-X^4C(O)R^{16}$ ,  $-X^4C(O)OR^{16}$ ,  $-X^4OC(O)R^{16}$ ,  $-X^4NR^{16}R^{17}$ ,  $-X^4NR^{17}C(O)R^{16}$ ,  
 $-X^4NR^{17}C(O)OR^{16}$ ,  $-X^4C(O)NR^{16}R^{17}$ ,  $-X^4S(O)_2NR^{16}R^{17}$ ,  $-X^4NR^{17}C(O)NR^{16}R^{17}$  or  
 $-X^4NR^{17}C(NR^{17})NR^{16}R^{17}$ , wherein  $X^4$ ,  $R^{16}$  and  $R^{17}$  are as defined above; wherein  
within  $R^9$  and/or  $R^{10}$  any alicyclic or aromatic ring system present may be substituted

further by 1 to 5 radicals independently selected from (C<sub>1-6</sub>)alkyl, (C<sub>1-6</sub>)alkylidene, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro, -X<sup>4</sup>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>OR<sup>12</sup>, -X<sup>4</sup>SR<sup>12</sup>, -X<sup>4</sup>C(O)OR<sup>12</sup>, -X<sup>4</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>P(O)(OR<sup>4</sup>)OR<sup>12</sup>, -X<sup>4</sup>OP(O)(OR<sup>12</sup>)OR<sup>12</sup>, -X<sup>4</sup>OC(O)R<sup>13</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)R<sup>13</sup>, -X<sup>4</sup>S(O)R<sup>13</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>13</sup> and -X<sup>4</sup>C(O)R<sup>13</sup>, wherein X<sup>4</sup>, R<sup>12</sup> and R<sup>13</sup> are as defined above, or

R<sup>9</sup> taken together with R<sup>7</sup> and/or R<sup>10</sup> taken together with R<sup>8</sup> form trimethylene, tetramethylene or phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene; and

R<sup>11</sup> is -X<sup>5</sup>X<sup>6</sup>R<sup>18</sup>, wherein X<sup>5</sup> is -C(O)-, -C(O)C(O)- or -S(O)<sub>2</sub>-, X<sup>6</sup> is a bond, -O- or -NR<sup>19</sup>-, wherein R<sup>19</sup> is hydrogen or (C<sub>1-6</sub>)alkyl, and R<sup>18</sup> is (i) (C<sub>1-10</sub>)alkyl optionally substituted by cyano, halo, nitro, -NR<sup>12</sup>R<sup>12</sup>, -NR<sup>12</sup>C(O)OR<sup>12</sup>, -NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -OR<sup>12</sup>, -SR<sup>12</sup>, -C(O)OR<sup>12</sup>, -C(O)NR<sup>12</sup>R<sup>12</sup>, -S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -P(O)(OR<sup>12</sup>)OR<sup>12</sup>, -OP(O)(OR<sup>12</sup>)OR<sup>12</sup>, -NR<sup>12</sup>C(O)R<sup>13</sup>, -S(O)R<sup>13</sup>, -S(O)<sub>2</sub>R<sup>13</sup>, -C(O)R<sup>13</sup>, -OR<sup>20</sup>, -SR<sup>20</sup>, -S(O)R<sup>20</sup>, -S(O)<sub>2</sub>R<sup>20</sup>, -C(O)R<sup>20</sup>, -C(O)OR<sup>20</sup>, -C(O)NR<sup>20</sup>R<sup>21</sup>, -NR<sup>20</sup>R<sup>21</sup>, -NR<sup>21</sup>C(O)R<sup>20</sup>, -NR<sup>21</sup>C(O)OR<sup>20</sup>, -NR<sup>21</sup>C(O)NR<sup>20</sup>R<sup>21</sup> or -NR<sup>21</sup>C(NR<sup>21</sup>)NR<sup>20</sup>R<sup>21</sup>, wherein R<sup>12</sup> and R<sup>13</sup> are as defined above, R<sup>20</sup> is (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-12</sub>)bicycloaryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>8-12</sub>)bicycloaryl(C<sub>0-6</sub>)alkyl and R<sup>21</sup> at each occurrence independently is hydrogen or (C<sub>1-6</sub>)alkyl, or (ii) (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-12</sub>)bicycloaryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>8-12</sub>)bicycloaryl(C<sub>0-6</sub>)alkyl or (iii) (C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, phenyl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl, wherein said cycloalkyl, heterocycloalkyl, phenyl or heteroaryl is substituted by -X<sup>4</sup>OR<sup>22</sup>, -X<sup>4</sup>SR<sup>22</sup>, -X<sup>4</sup>S(O)R<sup>22</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>22</sup>, -X<sup>4</sup>C(O)R<sup>22</sup>, -X<sup>4</sup>C(O)OR<sup>22</sup>, -X<sup>4</sup>C(O)NR<sup>22</sup>R<sup>23</sup>, -X<sup>4</sup>NR<sup>22</sup>R<sup>23</sup>, -X<sup>4</sup>NR<sup>23</sup>C(O)R<sup>22</sup>, -X<sup>4</sup>NR<sup>23</sup>C(O)OR<sup>22</sup>, -X<sup>4</sup>NR<sup>23</sup>C(O)NR<sup>22</sup>R<sup>23</sup> or -X<sup>4</sup>NR<sup>23</sup>C(NR<sup>23</sup>)NR<sup>22</sup>R<sup>23</sup>, wherein X<sup>4</sup> is as defined above,

$R^{22}$  is  $(C_{3-6})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-6})$ cycloalkyl $(C_{0-6})$ alkyl, phenyl $(C_{0-6})$ alkyl or hetero $(C_{5-6})$ aryl $(C_{0-6})$ alkyl and  $R^{23}$  at each occurrence independently is hydrogen or  $(C_{1-6})$ alkyl; wherein within  $R^{11}$  any alicyclic or aromatic ring system present may be substituted further by 1 to 5 radicals independently selected from  $(C_{1-6})$ alkyl,   
 5  $(C_{1-6})$ alkylidene, cyano, halo, halo-substituted  $(C_{1-4})$ alkyl, nitro,  $-X^4NR^{12}R^{12}$ ,  $-X^4NR^{12}C(O)OR^{12}$ ,  $-X^4NR^{12}C(O)NR^{12}R^{12}$ ,  $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-X^4OR^{12}$ ,  $-X^4SR^{12}$ ,  $-X^4C(O)OR^{12}$ ,  $-X^4C(O)NR^{12}R^{12}$ ,  $-X^4S(O)_2NR^{12}R^{12}$ ,  $-X^4P(O)(OR^3)OR^{12}$ ,  $-X^4OP(O)(OR^3)OR^{12}$ ,  $-X^4OC(O)R^{13}$ ,  $-X^4NR^{12}C(O)R^{13}$ ,  $-X^4S(O)R^{13}$ ,  $-X^4S(O)_2R^{13}$  and  $-X^4C(O)R^{13}$ , wherein  $X^4$ ,  $R^{12}$  and  $R^{13}$  are as defined above;

10  $R^2$  is hydrogen or  $(C_{1-6})$ alkyl or as defined below;

$R^3$  is hydrogen,  $(C_{1-6})$ alkyl or as defined below; and

$R^4$  is (i) hydrogen or  $(C_{1-6})$ alkyl, wherein said alkyl is optionally substituted with cyano, halo, nitro,  $-NR^{12}R^{12}$ ,  $-NR^{12}C(O)OR^{12}$ ,  $-NR^{12}C(O)NR^{12}R^{12}$ ,

$-NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-OR^{12}$ ,  $-SR^{12}$ ,  $-C(O)OR^{12}$ ,  $-C(O)NR^{12}R^{12}$ ,  $-S(O)_2NR^{12}R^{12}$ ,

15  $-P(O)(OR^{12})OR^{12}$ ,  $-OP(O)(OR^{12})OR^{12}$ ,  $-NR^{12}C(O)R^{13}$ ,  $-S(O)R^{13}$ ,  $-S(O)_2R^{13}$ ,  $-C(O)R^{13}$ ,

$-OR^{14}$ ,  $-SR^{14}$ ,  $-S(O)R^{14}$ ,  $-S(O)_2R^{14}$ ,  $-C(O)R^{14}$ ,  $-C(O)OR^{14}$ ,  $-OC(O)R^{14}$ ,  $-NR^{14}R^{15}$ ,

$-NR^{15}C(O)R^{14}$ ,  $-NR^{15}C(O)OR^{14}$ ,  $-C(O)NR^{14}R^{15}$ ,  $-S(O)_2NR^{14}R^{15}$ ,  $-NR^{15}C(O)NR^{14}R^{15}$  or

$-NR^{15}C(NR^{15})NR^{14}R^{15}$ , wherein  $R^{12}$ ,  $R^{13}$ ,  $R^{14}$  and  $R^{15}$  are as defined above, or (ii) a group selected from  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,

20  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  $(C_{9-12})$ polycycloaryl $(C_{0-6})$ alkyl and

hetero $(C_{8-12})$ polycycloaryl $(C_{0-6})$ alkyl, wherein said cycloalkyl, heterocycloalkyl, aryl,

heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a group

selected from  $-R^{16}$ ,  $-X^4OR^{16}$ ,  $-X^4SR^{16}$ ,  $-X^4S(O)R^{16}$ ,  $-X^4S(O)_2R^{16}$ ,  $-X^4C(O)R^{16}$ ,

$-X^4C(O)OR^{16}$ ,  $-X^4OC(O)R^{16}$ ,  $-X^4NR^{16}R^{17}$ ,  $-X^4NR^{17}C(O)R^{16}$ ,  $-X^4NR^{17}C(O)OR^{16}$ ,

25  $-X^4C(O)NR^{16}R^{17}$ ,  $-X^4S(O)_2NR^{16}R^{17}$ ,  $-X^4NR^{17}C(O)NR^{16}R^{17}$  or  $-X^4NR^{17}C(NR^{17})NR^{16}R^{17}$ ,

wherein  $X^4$ ,  $R^{16}$  and  $R^{17}$  are as defined above; wherein within  $R^9$  and/or  $R^{10}$  any alicyclic or aromatic ring system present may be substituted further by 1 to 5 radicals independently

selected from  $(C_{1-6})$ alkyl,  $(C_{1-6})$ alkylidene, cyano, halo, halo-substituted  $(C_{1-4})$ alkyl, nitro,

$-X^4NR^{12}R^{12}$ ,  $-X^4NR^{12}C(O)OR^{12}$ ,  $-X^4NR^{12}C(O)NR^{12}R^{12}$ ,  $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$ ,

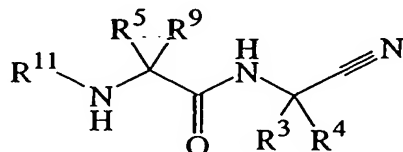
$-X^4OR^{12}$ ,  $-X^4SR^{12}$ ,  $-X^4C(O)OR^{12}$ ,  $-X^4C(O)NR^{12}R^{12}$ ,  $-X^4S(O)_2NR^{12}R^{12}$ ,  
 $-X^4P(O)(OR^3)OR^{12}$ ,  $-X^4OP(O)(OR^3)OR^{12}$ ,  $-X^4OC(O)R^{13}$ ,  $-X^4NR^{12}C(O)R^{13}$ ,  $-X^4S(O)R^{13}$ ,  
 $-X^4S(O)_2R^{13}$  and  $-X^4C(O)R^{13}$ , wherein  $X^4$ ,  $R^{12}$  and  $R^{13}$  are as defined above, or

$R^4$  and  $R^2$  taken together form trimethylene, tetramethylene or

5 phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene, or

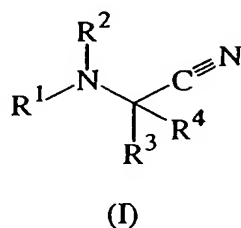
$R^4$  and  $R^3$  together with the carbon atom to which both  $R^4$  and  $R^3$  are attached form  
 $(C_{3-8})$ cycloalkylene or  $(C_{3-8})$ heterocycloalkylene; or an *N*-oxide derivative, prodrug  
derivative, individual isomer and mixtures of isomers; or a pharmaceutically acceptable salt  
thereof, but excluding compounds of the formula

10



in which  $R^3$  and  $R^4$  are each hydrogen or  $(C_{1-6})$ alkyl, or together with the carbon atom to  
which they are both attached form  $(C_{3-5})$ cycloalkylene;  $R^5$  is hydrogen or  $(C_{1-6})$ alkyl;  $R^9$  is  
 $(C_{6-12})$ aryl $(C_{1-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{1-6})$ alkyl,  $(C_{4-5})$ alkyl or cyclohexylmethyl; and  $R^{11}$  is  
 $C(O)R^{18}$  wherein  $R^{18}$  is hetero $(C_{3-12})$ cycloalkyl,  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl or hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl.  
15

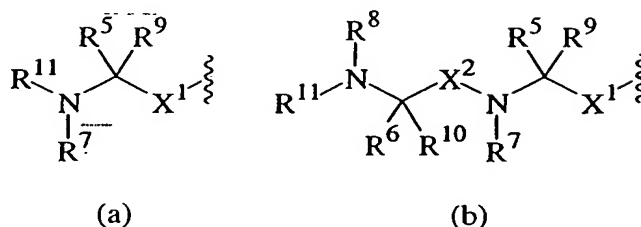
21. The use of a compound of Formula (I):



in which:

R<sup>1</sup> is a group of Formula (a) or (b):

5



wherein:

X<sup>1</sup> and X<sup>2</sup> independently are -C(O)- or -CH<sub>2</sub>S(O)<sub>2</sub>-;

R<sup>5</sup> and R<sup>6</sup> are hydrogen or (C<sub>1-6</sub>)alkyl;

R<sup>7</sup> and R<sup>8</sup> are hydrogen or (C<sub>1-6</sub>)alkyl or as defined below;

10

R<sup>9</sup> and R<sup>10</sup> independently are (i) (C<sub>1-6</sub>)alkyl optionally substituted with cyano,

halo or nitro or (ii) a group selected from -X<sup>3</sup>NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>,

-X<sup>3</sup>NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>OR<sup>12</sup>, -X<sup>3</sup>SR<sup>12</sup>,

-X<sup>3</sup>C(O)OR<sup>12</sup>, -X<sup>3</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>P(O)(OR<sup>12</sup>)OR<sup>12</sup>,

-X<sup>3</sup>OP(O)(OR<sup>12</sup>)OR<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)R<sup>13</sup>, -X<sup>3</sup>S(O)R<sup>13</sup>, -X<sup>3</sup>S(O)<sub>2</sub>R<sup>13</sup>, -X<sup>3</sup>C(O)R<sup>13</sup>,

15

-X<sup>3</sup>C(O)R<sup>14</sup>, -X<sup>3</sup>C(O)OR<sup>14</sup>, -X<sup>3</sup>OC(O)R<sup>14</sup>, -X<sup>3</sup>NR<sup>15</sup>C(O)R<sup>14</sup>, -X<sup>3</sup>NR<sup>15</sup>C(O)OR<sup>14</sup>,

-X<sup>3</sup>C(O)NR<sup>14</sup>R<sup>15</sup>, -X<sup>3</sup>S(O)<sub>2</sub>NR<sup>14</sup>R<sup>15</sup>, -X<sup>3</sup>NR<sup>15</sup>C(O)NR<sup>14</sup>R<sup>15</sup>,

-X<sup>3</sup>NR<sup>15</sup>C(NR<sup>15</sup>)NR<sup>14</sup>R<sup>15</sup>, -X<sup>4</sup>SR<sup>14</sup> -X<sup>4</sup>S(O)R<sup>14</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>14</sup>, -X<sup>4</sup>OR<sup>14</sup>, or

-X<sup>4</sup>NR<sup>14</sup>R<sup>15</sup>, wherein X<sup>3</sup> is (C<sub>1-6</sub>)alkylene, X<sup>4</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>12</sup> at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl, R<sup>13</sup>

20

is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-3</sub>)alkyl, R<sup>14</sup> is (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl,

hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl,



(C<sub>9-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>8-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl and R<sup>15</sup> is hydrogen or (C<sub>1-6</sub>)alkyl, and wherein within R<sup>14</sup> said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a group selected from -R<sup>16</sup>, -X<sup>4</sup>OR<sup>16</sup>, -X<sup>4</sup>SR<sup>16</sup>, -X<sup>4</sup>S(O)R<sup>16</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>16</sup>,  
5 -X<sup>4</sup>C(O)R<sup>16</sup>, -X<sup>4</sup>C(O)OR<sup>16</sup>, -X<sup>4</sup>OC(O)R<sup>16</sup>, -X<sup>4</sup>NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)R<sup>16</sup>,  
-X<sup>4</sup>NR<sup>17</sup>C(O)OR<sup>16</sup>, -X<sup>4</sup>C(O)NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>S(O)<sub>2</sub>NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)NR<sup>16</sup>R<sup>17</sup> or  
-X<sup>4</sup>NR<sup>17</sup>C(NR<sup>17</sup>)NR<sup>16</sup>R<sup>17</sup>, wherein X<sup>4</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>16</sup> is hydrogen or (C<sub>1-6</sub>)alkyl and R<sup>17</sup> is (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl or  
10 hetero(C<sub>8-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl, or (iii) a group selected from  
(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl and  
hetero(C<sub>8-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl, wherein said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a  
15 group selected from -R<sup>16</sup>, -X<sup>4</sup>OR<sup>16</sup>, -X<sup>4</sup>SR<sup>16</sup>, -X<sup>4</sup>S(O)R<sup>16</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>16</sup>,  
-X<sup>4</sup>C(O)R<sup>16</sup>, -X<sup>4</sup>C(O)OR<sup>16</sup>, -X<sup>4</sup>OC(O)R<sup>16</sup>, -X<sup>4</sup>NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)R<sup>16</sup>,  
-X<sup>4</sup>NR<sup>17</sup>C(O)OR<sup>16</sup>, -X<sup>4</sup>C(O)NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>S(O)<sub>2</sub>NR<sup>16</sup>R<sup>17</sup>, -X<sup>4</sup>NR<sup>17</sup>C(O)NR<sup>16</sup>R<sup>17</sup> or  
-X<sup>4</sup>NR<sup>17</sup>C(NR<sup>17</sup>)NR<sup>16</sup>R<sup>17</sup>, wherein X<sup>4</sup>, R<sup>16</sup> and R<sup>17</sup> are as defined above; wherein  
within R<sup>9</sup> and/or R<sup>10</sup> any alicyclic or aromatic ring system present may be substituted  
20 further by 1 to 5 radicals independently selected from (C<sub>1-6</sub>)alkyl, (C<sub>1-6</sub>)alkylidene, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro, -X<sup>4</sup>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>,  
-X<sup>4</sup>NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>OR<sup>12</sup>, -X<sup>4</sup>SR<sup>12</sup>,  
-X<sup>4</sup>C(O)OR<sup>12</sup>, -X<sup>4</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>P(O)(OR<sup>4</sup>)OR<sup>12</sup>,  
-X<sup>4</sup>OP(O)(OR<sup>12</sup>)OR<sup>12</sup>, -X<sup>4</sup>OC(O)R<sup>13</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)R<sup>13</sup>, -X<sup>4</sup>S(O)R<sup>13</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>13</sup>  
25 and -X<sup>4</sup>C(O)R<sup>13</sup>, wherein X<sup>4</sup>, R<sup>12</sup> and R<sup>13</sup> are as defined above, or

R<sup>9</sup> taken together with R<sup>7</sup> and/or R<sup>10</sup> taken together with R<sup>8</sup> form trimethylene, tetramethylene or phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene; and

R<sup>11</sup> is -X<sup>5</sup>X<sup>6</sup>R<sup>18</sup>, wherein X<sup>5</sup> is -C(O)-, -C(O)C(O)- or -S(O)<sub>2</sub>-, X<sup>6</sup> is a

bond, -O- or -NR<sup>19</sup>-, wherein R<sup>19</sup> is hydrogen or (C<sub>1-6</sub>)alkyl, and R<sup>18</sup> is

(i) (C<sub>1-10</sub>)alkyl optionally substituted by cyano, halo, nitro, -NR<sup>12</sup>R<sup>12</sup>,  
-NR<sup>12</sup>C(O)OR<sup>12</sup>, -NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -OR<sup>12</sup>, -SR<sup>12</sup>,  
-C(O)OR<sup>12</sup>, -C(O)NR<sup>12</sup>R<sup>12</sup>, -S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -P(O)(OR<sup>12</sup>)OR<sup>12</sup>,

5 -OP(O)(OR<sup>12</sup>)OR<sup>12</sup>, -NR<sup>12</sup>C(O)R<sup>13</sup>, -S(O)R<sup>13</sup>, -S(O)<sub>2</sub>R<sup>13</sup>, -C(O)R<sup>13</sup>, -OR<sup>20</sup>, -SR<sup>20</sup>,  
-S(O)R<sup>20</sup>, -S(O)<sub>2</sub>R<sup>20</sup>, -C(O)R<sup>20</sup>, -C(O)OR<sup>20</sup>, -C(O)NR<sup>20</sup>R<sup>21</sup>, -NR<sup>20</sup>R<sup>21</sup>,  
-NR<sup>21</sup>C(O)R<sup>20</sup>, -NR<sup>21</sup>C(O)OR<sup>20</sup>, -NR<sup>21</sup>C(O)NR<sup>20</sup>R<sup>21</sup> or -NR<sup>21</sup>C(NR<sup>21</sup>)NR<sup>20</sup>R<sup>21</sup>,

wherein R<sup>12</sup> and R<sup>13</sup> are as defined above, R<sup>20</sup> is (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl,

hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl,

10 (C<sub>9-12</sub>)bicycloaryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>8-12</sub>)bicycloaryl(C<sub>0-6</sub>)alkyl and R<sup>21</sup> at each  
occurrence independently is hydrogen or (C<sub>1-6</sub>)alkyl, or

(ii) (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl,  
(C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-12</sub>)bicycloaryl(C<sub>0-6</sub>)alkyl or  
hetero(C<sub>8-12</sub>)bicycloaryl(C<sub>0-6</sub>)alkyl or (iii) (C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl,

15 hetero(C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, phenyl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl,  
wherein said cycloalkyl, heterocycloalkyl, phenyl or heteroaryl is substituted by

-X<sup>4</sup>OR<sup>22</sup>, -X<sup>4</sup>SR<sup>22</sup>, -X<sup>4</sup>S(O)R<sup>22</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>22</sup>, -X<sup>4</sup>C(O)R<sup>22</sup>, -X<sup>4</sup>C(O)OR<sup>22</sup>,  
-X<sup>4</sup>C(O)NR<sup>22</sup>R<sup>23</sup>, -X<sup>4</sup>NR<sup>22</sup>R<sup>23</sup>, -X<sup>4</sup>NR<sup>23</sup>C(O)R<sup>22</sup>, -X<sup>4</sup>NR<sup>23</sup>C(O)OR<sup>22</sup>,  
-X<sup>4</sup>NR<sup>23</sup>C(O)NR<sup>22</sup>R<sup>23</sup> or -X<sup>4</sup>NR<sup>23</sup>C(NR<sup>23</sup>)NR<sup>22</sup>R<sup>23</sup>, wherein X<sup>4</sup> is as defined above,

20 R<sup>22</sup> is (C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, phenyl(C<sub>0-6</sub>)alkyl  
or hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl and R<sup>23</sup> at each occurrence independently is hydrogen  
or (C<sub>1-6</sub>)alkyl; wherein within R<sup>11</sup> any alicyclic or aromatic ring system present may be

substituted further by 1 to 5 radicals independently selected from (C<sub>1-6</sub>)alkyl,  
(C<sub>1-6</sub>)alkylidene, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro, -X<sup>4</sup>NR<sup>12</sup>R<sup>12</sup>,

25 -X<sup>4</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>OR<sup>12</sup>,  
-X<sup>4</sup>SR<sup>12</sup>, -X<sup>4</sup>C(O)OR<sup>12</sup>, -X<sup>4</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -X<sup>4</sup>P(O)(OR<sup>3</sup>)OR<sup>12</sup>,  
-X<sup>4</sup>OP(O)(OR<sup>3</sup>)OR<sup>12</sup>, -X<sup>4</sup>OC(O)R<sup>13</sup>, -X<sup>4</sup>NR<sup>12</sup>C(O)R<sup>13</sup>, -X<sup>4</sup>S(O)R<sup>13</sup>, -X<sup>4</sup>S(O)<sub>2</sub>R<sup>13</sup>  
and -X<sup>4</sup>C(O)R<sup>13</sup>, wherein X<sup>4</sup>, R<sup>12</sup> and R<sup>13</sup> are as defined above;

R<sup>2</sup> is hydrogen or (C<sub>1-6</sub>)alkyl or as defined below;

$R^3$  is hydrogen,  $(C_{1-6})$ alkyl or as defined below; and

$R^4$  is (i) hydrogen or  $(C_{1-6})$ alkyl, wherein said alkyl is optionally substituted with cyano, halo, nitro,  $-NR^{12}R^{12}$ ,  $-NR^{12}C(O)OR^{12}$ ,  $-NR^{12}C(O)NR^{12}R^{12}$ ,

$-NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-OR^{12}$ ,  $-SR^{12}$ ,  $-C(O)OR^{12}$ ,  $-C(O)NR^{12}R^{12}$ ,  $-S(O)_2NR^{12}R^{12}$ ,

5  $-P(O)(OR^{12})OR^{12}$ ,  $-OP(O)(OR^{12})OR^{12}$ ,  $-NR^{12}C(O)R^{13}$ ,  $-S(O)R^{13}$ ,  $-S(O)_2R^{13}$ ,  $-C(O)R^{13}$ ,

$-OR^{14}$ ,  $-SR^{14}$ ,  $-S(O)R^{14}$ ,  $-S(O)_2R^{14}$ ,  $-C(O)R^{14}$ ,  $-C(O)OR^{14}$ ,  $-OC(O)R^{14}$ ,  $-NR^{14}R^{15}$ ,

$-NR^{15}C(O)R^{14}$ ,  $-NR^{15}C(O)OR^{14}$ ,  $-C(O)NR^{14}R^{15}$ ,  $-S(O)_2NR^{14}R^{15}$ ,  $-NR^{15}C(O)NR^{14}R^{15}$  or

$-NR^{15}C(NR^{15})NR^{14}R^{15}$ , wherein  $R^{12}$ ,  $R^{13}$ ,  $R^{14}$  and  $R^{15}$  are as defined above, or (ii) a group

selected from  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, ———

10  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  $(C_{9-12})$ polycycloaryl $(C_{0-6})$ alkyl and

hetero $(C_{8-12})$ polycycloaryl $(C_{0-6})$ alkyl; wherein said cycloalkyl, heterocycloalkyl, aryl,

heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a group

selected from  $-R^{16}$ ,  $-X^4OR^{16}$ ,  $-X^4SR^{16}$ ,  $-X^4S(O)R^{16}$ ,  $-X^4S(O)_2R^{16}$ ,  $-X^4C(O)R^{16}$ ,

$-X^4C(O)OR^{16}$ ,  $-X^4OC(O)R^{16}$ ,  $-X^4NR^{16}R^{17}$ ,  $-X^4NR^{17}C(O)R^{16}$ ,  $-X^4NR^{17}C(O)OR^{16}$ ,

15  $-X^4C(O)NR^{16}R^{17}$ ,  $-X^4S(O)_2NR^{16}R^{17}$ ,  $-X^4NR^{17}C(O)NR^{16}R^{17}$  or  $-X^4NR^{17}C(NR^{17})NR^{16}R^{17}$ ,

wherein  $X^4$ ,  $R^{16}$  and  $R^{17}$  are as defined above; wherein within  $R^9$  and/or  $R^{10}$  any alicyclic or aromatic ring system present may be substituted further by 1 to 5 radicals independently

selected from  $(C_{1-6})$ alkyl,  $(C_{1-6})$ alkylidene, cyano, halo, halo-substituted  $(C_{1-4})$ alkyl, nitro,

$-X^4NR^{12}R^{12}$ ,  $-X^4NR^{12}C(O)OR^{12}$ ,  $-X^4NR^{12}C(O)NR^{12}R^{12}$ ,  $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$ ,

20  $-X^4OR^{12}$ ,  $-X^4SR^{12}$ ,  $-X^4C(O)OR^{12}$ ,  $-X^4C(O)NR^{12}R^{12}$ ,  $-X^4S(O)_2NR^{12}R^{12}$ ,

$-X^4P(O)(OR^3)OR^{12}$ ,  $-X^4OP(O)(OR^3)OR^{12}$ ,  $-X^4OC(O)R^{13}$ ,  $-X^4NR^{12}C(O)R^{13}$ ,  $-X^4S(O)R^{13}$ ,

$-X^4S(O)_2R^{13}$  and  $-X^4C(O)R^{13}$ , wherein  $X^4$ ,  $R^{12}$  and  $R^{13}$  are as defined above, or

$R^4$  and  $R^2$  taken together form trimethylene, tetramethylene or

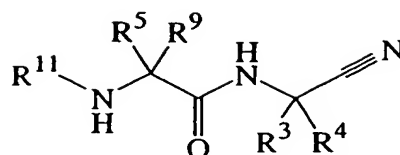
phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene, or

25  $R^4$  and  $R^3$  together with the carbon atom to which both  $R^4$  and  $R^3$  are attached form

$(C_{3-8})$ cycloalkylene or  $(C_{3-8})$ heterocycloalkylene; or an *N*-oxide derivative, prodrug

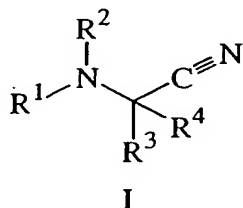
derivative, individual isomer and mixtures of isomers; or a pharmaceutically acceptable salt

thereof, but excluding compounds of the formula



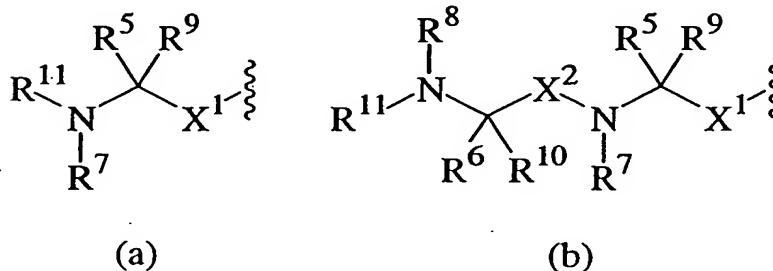
- in which R<sup>3</sup> and R<sup>4</sup> are each hydrogen or (C<sub>1-6</sub>)alkyl, or together with the carbon atom to which they are both attached form (C<sub>3-5</sub>)cycloalkylene; R<sup>5</sup> is hydrogen or (C<sub>1-6</sub>)alkyl; R<sup>9</sup> is (C<sub>6-12</sub>)aryl(C<sub>1-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>1-6</sub>)alkyl, (C<sub>4-5</sub>)alkyl or cyclohexylmethyl; and R<sup>11</sup> is C(O)R<sup>18</sup> wherein R<sup>18</sup> is hetero(C<sub>3-12</sub>)cycloalkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, in the manufacture of a medicament for treating a disease in an animal in which cathepsin S activity contributes to the pathology and/or symptomatology of the disease.

22. A process for preparing a compound of Formula I:



- 10 in which:

R<sup>1</sup> is a group of Formula (a) or (b):



wherein:

X<sup>1</sup> and X<sup>2</sup> independently are -C(O)- or -CH<sub>2</sub>S(O)<sub>2</sub>-;

R<sup>5</sup> and R<sup>6</sup> are hydrogen or (C<sub>1-6</sub>)alkyl;

$R^7$  and  $R^8$  are hydrogen or  $(C_{1-6})$ alkyl or as defined below;

$R^9$  and  $R^{10}$  independently are (i)  $(C_{1-6})$ alkyl optionally substituted with cyano, halo, nitro,  $-NR^{12}R^{12}$ ,  $-NR^{12}C(O)OR^{12}$ ,  $-NR^{12}C(O)NR^{12}R^{12}$ ,  $-NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-OR^{12}$ ,  $-SR^{12}$ ,  $-C(O)OR^{12}$ ,  $-C(O)NR^{12}R^{12}$ ,  $-S(O)_2NR^{12}R^{12}$ ,  $-P(O)(OR^{12})OR^{12}$ ,  $-OP(O)(OR^{12})OR^{12}$ ,  $-NR^{12}C(O)R^{13}$ ,  $-S(O)R^{13}$ ,  $-S(O)_2R^{13}$ ,  $-C(O)R^{13}$ ,  $-OR^{14}$ ,  $-SR^{14}$ ,  $-S(O)R^{14}$ ,  $-S(O)_2R^{14}$ ,  $-C(O)R^{14}$ ,  $-C(O)OR^{14}$ ,  $-OC(O)R^{14}$ ,  $-NR^{14}R^{15}$ ,  $-NR^{15}C(O)R^{14}$ ,  $-NR^{15}C(O)OR^{14}$ ,  $-C(O)NR^{14}R^{15}$ ,  $-S(O)_2NR^{14}R^{15}$ ,  $-NR^{15}C(O)NR^{14}R^{15}$  or  $-NR^{15}C(NR^{15})NR^{14}R^{15}$ , wherein  $R^{12}$  at each occurrence independently is hydrogen,  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-3})$ alkyl,  $R^{13}$  is  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-3})$ alkyl,  $R^{14}$  is  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  $(C_{9-12})$ polycycloaryl $(C_{0-6})$ alkyl or hetero $(C_{8-12})$ polycycloaryl $(C_{0-6})$ alkyl and  $R^{15}$  is hydrogen or  $(C_{1-6})$ alkyl, and wherein within  $R^{14}$  said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a group selected from  $-R^{16}$ ,  $-X^3OR^{16}$ ,  $-X^3SR^{16}$ ,  $-X^3S(O)R^{16}$ ,  $-X^3S(O)_2R^{16}$ ,  $-X^3C(O)R^{16}$ ,  $-X^3C(O)OR^{16}$ ,  $-X^3OC(O)R^{16}$ ,  $-X^3NR^{16}R^{17}$ ,  $-X^3NR^{17}C(O)R^{16}$ ,  $-X^3NR^{17}C(O)OR^{16}$ ,  $-X^3C(O)NR^{16}R^{17}$ ,  $-X^3S(O)_2NR^{16}R^{17}$ ,  $-X^3NR^{17}C(O)NR^{16}R^{17}$  or  $-X^3NR^{17}C(NR^{17})NR^{16}R^{17}$ , wherein  $X^3$  is a bond or  $(C_{1-6})$ alkylene,  $R^{16}$  is hydrogen or  $(C_{1-6})$ alkyl and  $R^{17}$  is  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  $(C_{9-12})$ polycycloaryl $(C_{0-6})$ alkyl or hetero $(C_{8-12})$ polycycloaryl $(C_{0-6})$ alkyl, or (ii) a group selected from  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  $(C_{9-12})$ polycycloaryl $(C_{0-6})$ alkyl and hetero $(C_{8-12})$ polycycloaryl $(C_{0-6})$ alkyl, wherein said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a group selected from  $-R^{16}$ ,  $-X^3OR^{16}$ ,  $-X^3SR^{16}$ ,  $-X^3S(O)R^{16}$ ,  $-X^3S(O)_2R^{16}$ ,  $-X^3C(O)R^{16}$ ,  $-X^3C(O)OR^{16}$ ,  $-X^3OC(O)R^{16}$ ,  $-X^3NR^{16}R^{17}$ ,  $-X^3NR^{17}C(O)R^{16}$ ,  $-X^3NR^{17}C(O)OR^{16}$ ,  $-X^3C(O)NR^{16}R^{17}$ ,  $-X^3S(O)_2NR^{16}R^{17}$ ,  $-X^3NR^{17}C(O)NR^{16}R^{17}$  or  $-X^3NR^{17}C(NR^{17})NR^{16}R^{17}$ , wherein  $X^3$ ,  $R^{16}$  and  $R^{17}$  are as defined above; wherein

within  $R^9$  and/or  $R^{10}$  any alicyclic or aromatic ring system present may be substituted further by 1 to 5 radicals independently selected from  $(C_{1-6})$ alkyl,  $(C_{1-6})$ alkylidene, cyano, halo, halo-substituted  $(C_{1-4})$ alkyl, nitro,  $-X^3NR^{12}R^{12}$ ,  $-X^3NR^{12}C(O)OR^{12}$ ,  $-X^3NR^{12}C(O)NR^{12}R^{12}$ ,  $-X^3NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-X^3OR^{12}$ ,  $-X^3SR^{12}$ ,  
 5  $-X^3C(O)OR^{12}$ ,  $-X^3C(O)NR^{12}R^{12}$ ,  $-X^3S(O)_2NR^{12}R^{12}$ ,  $-X^3P(O)(OR^3)OR^{12}$ ,  $-X^3OP(O)(OR^3)OR^{12}$ ,  $-X^3OC(O)R^{13}$ ,  $-X^3NR^{12}C(O)R^{13}$ ,  $-X^3S(O)R^{13}$ ,  $-X^3S(O)_2R^{13}$  and  $-X^3C(O)R^{13}$ , wherein  $X^3$ ,  $R^{12}$  and  $R^{13}$  are as defined above, or

$R^9$  taken together with  $R^7$  and/or  $R^{10}$  taken together with  $R^8$  form trimethylene, tetramethylene or phenylene-1,2-dimethylene, optionally substituted with  
 10 hydroxy, oxo or methylene; and

$R^{11}$  is  $-X^4X^5R^{18}$ , wherein  $X^4$  is  $-C(O)-$ ,  $-C(O)C(O)-$  or  $-S(O)_2-$ ,  $X^5$  is a bond,  $-O-$  or  $-NR^{19}-$ , wherein  $R^{19}$  is hydrogen or  $(C_{1-6})$ alkyl, and  $R^{18}$  is

(i)  $(C_{1-10})$ alkyl optionally substituted by cyano, halo, nitro,  $-NR^{12}R^{12}$ ,  $-NR^{12}C(O)OR^{12}$ ,  $-NR^{12}C(O)NR^{12}R^{12}$ ,  $-NR^{12}C(NR^{12})NR^{12}R^{12}$ ,  $-OR^{12}$ ,  $-SR^{12}$ ,  
 15  $-C(O)OR^{12}$ ,  $-C(O)NR^{12}R^{12}$ ,  $-S(O)_2NR^{12}R^{12}$ ,  $-P(O)(OR^{12})OR^{12}$ ,  $-OP(O)(OR^{12})OR^{12}$ ,  $-NR^{12}C(O)R^{13}$ ,  $-S(O)R^{13}$ ,  $-S(O)_2R^{13}$ ,  $-C(O)R^{13}$ ,  $-OR^{20}$ ,  $-SR^{20}$ ,  $-S(O)R^{20}$ ,  $-S(O)_2R^{20}$ ,  $-C(O)R^{20}$ ,  $-C(O)OR^{20}$ ,  $-C(O)NR^{20}R^{21}$ ,  $-NR^{20}R^{21}$ ,  $-NR^{21}C(O)R^{20}$ ,  $-NR^{21}C(O)OR^{20}$ ,  $-NR^{21}C(O)NR^{20}R^{21}$  or  $-NR^{21}C(NR^{21})NR^{20}R^{21}$ , wherein  $R^{12}$  and  $R^{13}$  are as defined above,  $R^{20}$  is  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  
 20 hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  $(C_{9-12})$ bicycloaryl $(C_{0-6})$ alkyl or hetero $(C_{8-12})$ bicycloaryl $(C_{0-6})$ alkyl and  $R^{21}$  at each occurrence independently is hydrogen or  $(C_{1-6})$ alkyl, or

(ii)  $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-12})$ cycloalkyl $(C_{0-6})$ alkyl,  $(C_{6-12})$ aryl $(C_{0-6})$ alkyl, hetero $(C_{5-12})$ aryl $(C_{0-6})$ alkyl,  $(C_{9-12})$ bicycloaryl $(C_{0-6})$ alkyl or  
 25 hetero $(C_{8-12})$ bicycloaryl $(C_{0-6})$ alkyl or (iii)  $(C_{3-6})$ cycloalkyl $(C_{0-6})$ alkyl, hetero $(C_{3-6})$ cycloalkyl $(C_{0-6})$ alkyl, phenyl $(C_{0-6})$ alkyl or hetero $(C_{5-6})$ aryl $(C_{0-6})$ alkyl, wherein said cycloalkyl, heterocycloalkyl, phenyl or heteroaryl is substituted by  $-X^3OR^{22}$ ,  $-X^3SR^{22}$ ,  $-X^3S(O)R^{22}$ ,  $-X^3S(O)_2R^{22}$ ,  $-X^3C(O)R^{22}$ ,  $-X^3C(O)OR^{22}$ ,  $-X^3C(O)NR^{22}R^{23}$ ,  $-X^3NR^{22}R^{23}$ ,  $-X^3NR^{23}C(O)R^{22}$ ,  $-X^3NR^{23}C(O)OR^{22}$ ,

-X<sup>3</sup>NR<sup>23</sup>C(O)NR<sup>22</sup>R<sup>23</sup> or -X<sup>3</sup>NR<sup>23</sup>C(NR<sup>23</sup>)NR<sup>22</sup>R<sup>23</sup>, wherein X<sup>3</sup> is as defined above, R<sup>22</sup> is (C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-6</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, phenyl(C<sub>0-6</sub>)alkyl or hetero(C<sub>5-6</sub>)aryl(C<sub>0-6</sub>)alkyl and R<sup>23</sup> at each occurrence independently is hydrogen or (C<sub>1-6</sub>)alkyl; wherein within R<sup>11</sup> any alicyclic or aromatic ring system present may be substituted further by 1 to 5 radicals independently selected from (C<sub>1-6</sub>)alkyl, (C<sub>1-6</sub>)alkylidene, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro, -X<sup>3</sup>NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>OR<sup>12</sup>, -X<sup>3</sup>SR<sup>12</sup>, -X<sup>3</sup>C(O)OR<sup>12</sup>, -X<sup>3</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>P(O)(OR<sup>3</sup>)OR<sup>12</sup>, -X<sup>3</sup>OP(O)(OR<sup>3</sup>)OR<sup>12</sup>, -X<sup>3</sup>OC(O)R<sup>13</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)R<sup>13</sup>, -X<sup>3</sup>S(O)R<sup>13</sup>, -X<sup>3</sup>S(O)<sub>2</sub>R<sup>13</sup> and -X<sup>3</sup>C(O)R<sup>13</sup>, wherein X<sup>3</sup>, R<sup>12</sup> and R<sup>13</sup> are as defined above;

R<sup>2</sup> is hydrogen or (C<sub>1-6</sub>)alkyl or as defined below;

R<sup>3</sup> is hydrogen, (C<sub>1-6</sub>)alkyl or as defined below; and

R<sup>4</sup> is (i) hydrogen or (C<sub>1-6</sub>)alkyl, wherein said alkyl is optionally substituted with cyano, halo, nitro, -NR<sup>12</sup>R<sup>12</sup>, -NR<sup>12</sup>C(O)OR<sup>12</sup>, -NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>,

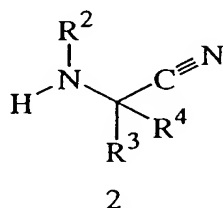
-NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>, -OR<sup>12</sup>, -SR<sup>12</sup>, -C(O)OR<sup>12</sup>, -C(O)NR<sup>12</sup>R<sup>12</sup>, -S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>, -P(O)(OR<sup>12</sup>)OR<sup>12</sup>, -OP(O)(OR<sup>12</sup>)OR<sup>12</sup>, -NR<sup>12</sup>C(O)R<sup>13</sup>, -S(O)R<sup>13</sup>, -S(O)<sub>2</sub>R<sup>13</sup>, -C(O)R<sup>13</sup>, -OR<sup>14</sup>, -SR<sup>14</sup>, -S(O)R<sup>14</sup>, -S(O)<sub>2</sub>R<sup>14</sup>, -C(O)R<sup>14</sup>, -C(O)OR<sup>14</sup>, -OC(O)R<sup>14</sup>, -NR<sup>14</sup>R<sup>15</sup>, -NR<sup>15</sup>C(O)R<sup>14</sup>, -NR<sup>15</sup>C(O)OR<sup>14</sup>, -C(O)NR<sup>14</sup>R<sup>15</sup>, -S(O)<sub>2</sub>NR<sup>14</sup>R<sup>15</sup>, -NR<sup>15</sup>C(O)NR<sup>14</sup>R<sup>15</sup> or -NR<sup>15</sup>C(NR<sup>15</sup>)NR<sup>14</sup>R<sup>15</sup>, wherein R<sup>12</sup>, R<sup>13</sup>, R<sup>14</sup> and R<sup>15</sup> are as defined above, or (ii) a group

selected from (C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, hetero(C<sub>3-12</sub>)cycloalkyl(C<sub>0-6</sub>)alkyl, (C<sub>6-12</sub>)aryl(C<sub>0-6</sub>)alkyl, hetero(C<sub>5-12</sub>)aryl(C<sub>0-6</sub>)alkyl, (C<sub>9-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl and hetero(C<sub>8-12</sub>)polycycloaryl(C<sub>0-6</sub>)alkyl, wherein said cycloalkyl, heterocycloalkyl, aryl, heteroaryl, polycycloaryl or heteropolycycloaryl ring optionally is substituted by a group selected from -R<sup>16</sup>, -X<sup>3</sup>OR<sup>16</sup>, -X<sup>3</sup>SR<sup>16</sup>, -X<sup>3</sup>S(O)R<sup>16</sup>, -X<sup>3</sup>S(O)<sub>2</sub>R<sup>16</sup>, -X<sup>3</sup>C(O)R<sup>16</sup>,

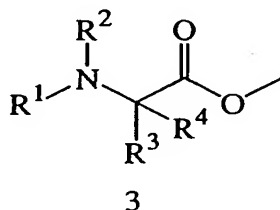
-X<sup>3</sup>C(O)OR<sup>16</sup>, -X<sup>3</sup>OC(O)R<sup>16</sup>, -X<sup>3</sup>NR<sup>16</sup>R<sup>17</sup>, -X<sup>3</sup>NR<sup>17</sup>C(O)R<sup>16</sup>, -X<sup>3</sup>NR<sup>17</sup>C(O)OR<sup>16</sup>, -X<sup>3</sup>C(O)NR<sup>16</sup>R<sup>17</sup>, -X<sup>3</sup>S(O)<sub>2</sub>NR<sup>16</sup>R<sup>17</sup>, -X<sup>3</sup>NR<sup>17</sup>C(O)NR<sup>16</sup>R<sup>17</sup> or -X<sup>3</sup>NR<sup>17</sup>C(NR<sup>17</sup>)NR<sup>16</sup>R<sup>17</sup>, wherein X<sup>3</sup>, R<sup>16</sup> and R<sup>17</sup> are as defined above; wherein within R<sup>9</sup> and/or R<sup>10</sup> any alicyclic or aromatic ring system present may be substituted further by 1 to 5 radicals independently selected from (C<sub>1-6</sub>)alkyl, (C<sub>1-6</sub>)alkylidene, cyano, halo, halo-substituted (C<sub>1-4</sub>)alkyl, nitro,

-X<sup>3</sup>NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)OR<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>NR<sup>12</sup>C(NR<sup>12</sup>)NR<sup>12</sup>R<sup>12</sup>,  
 -X<sup>3</sup>OR<sup>12</sup>, -X<sup>3</sup>SR<sup>12</sup>, -X<sup>3</sup>C(O)OR<sup>12</sup>, -X<sup>3</sup>C(O)NR<sup>12</sup>R<sup>12</sup>, -X<sup>3</sup>S(O)<sub>2</sub>NR<sup>12</sup>R<sup>12</sup>,  
 -X<sup>3</sup>P(O)(OR<sup>3</sup>)OR<sup>12</sup>, -X<sup>3</sup>OP(O)(OR<sup>3</sup>)OR<sup>12</sup>, -X<sup>3</sup>OC(O)R<sup>13</sup>, -X<sup>3</sup>NR<sup>12</sup>C(O)R<sup>13</sup>, -X<sup>3</sup>S(O)R<sup>13</sup>,  
 -X<sup>3</sup>S(O)<sub>2</sub>R<sup>13</sup> and -X<sup>3</sup>C(O)R<sup>13</sup>, wherein X<sup>3</sup>, R<sup>12</sup> and R<sup>13</sup> are as defined above, or

- 5           R<sup>4</sup> and R<sup>2</sup> taken together form trimethylene, tetramethylene or  
 phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene, or  
             R<sup>4</sup> and R<sup>3</sup> together with the carbon atom to which both R<sup>4</sup> and R<sup>3</sup> are attached form  
 (C<sub>3-8</sub>)cycloalkylene or (C<sub>3-8</sub>)heterocycloalkylene; and the *N*-oxide derivatives, prodrug  
 derivatives, protected derivatives, individual isomers and mixtures of isomers; and the  
 10   pharmaceutically acceptable salts thereof; which process comprises:  
 (A)   reacting a compound of Formula 2:



- or a protected derivative thereof, with a compound of the formula R<sup>1</sup>OY, or a protected  
 derivative thereof, in which Y is hydrogen or 2,5-dioxopyrrolidin-1-yl and each R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>  
 15   and R<sup>4</sup> are as defined above; or  
 (B)   reacting a compound of Formula 3:



- or a protected derivative thereof, with ammonia to provide a corresponding amide and then  
 reacting the amide with trifluoroacetic anhydride, in which each R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are as  
 20   defined above;



- (C) optionally deprotecting a protected derivative of a compound of Formula I to provide a corresponding unprotected derivative;
- (D) optionally converting a compound of Formula I into a pharmaceutically acceptable salt;
- 5 (E) optionally converting a salt form of a compound of Formula I to non-salt form;
- (F) optionally converting an unoxidized form of a compound of Formula I into a pharmaceutically acceptable *N*-oxide;
- (G) optionally converting an *N*-oxide form of a compound of Formula I to its unoxidized form;
- 10 (H) optionally converting a non-derivatized compound of Formula I into a pharmaceutically prodrug derivative; and
- (I) optionally converting a prodrug derivative of a compound of Formula I to its non-derivatized form.